SUMMARY OF SAFETY AND EFFECTIVENESS DATA (SSED)

I. GENERAL INFORMATION

Device Generic Name: Endovascular Graft

Device Trade Name: TREO® Abdominal Stent-Graft System

Device Procode: MIH

Applicant's Name and Address: Bolton Medical, Inc.
799 International Parkway
Sunrise, FL 33325
USA

Date(s) of Panel Recommendation: None

Premarket Approval Application (PMA) Number: P190015

Date of FDA Notice of Approval: May 4, 2020

II. INDICATIONS FOR USE

The TREO® Abdominal Stent-Graft System is indicated for use in the endovascular treatment of patients with infrarenal abdominal aortic and aorto-iliac aneurysms with the following characteristics:

- Adequate iliac or femoral access compatible with the required delivery systems and accessories
- Proximal aortic landing zone with:
  - Infrarenal landing neck length of ≥ 15mm
  - Aortic neck diameters ≥ 17 mm and ≤ 32 mm
  - Suprarenal neck angle of ≤ 45 degrees
  - Infrarenal neck angle of ≤ 60 degrees
- Distal iliac landing zone with:
  - an inside diameter of 8 mm – 13 mm and a length of ≥ 10 mm or
  - an inside diameter of > 13 mm – 20 mm and a length of ≥ 15 mm
- Minimum overall AAA treatment length (proximal landing location to distal landing location) of 13 cm
- Minimum overall length from the lowest renal artery to the aortic bifurcation of 9 cm

III. CONTRAINDICATIONS

The TREO® Abdominal Stent-Graft System is contraindicated in the following:

- Patients with a known allergy or intolerance to device materials (nitinol, polyester, platinum-iridium).
- Patients with a condition that threatens to infect the graft.

IV. WARNINGS AND PRECAUTIONS

The warnings and precautions can be found in the TREO® Abdominal Stent-Graft System labeling.

V. DEVICE DESCRIPTION

The TREO® Abdominal Stent-Graft System (referred to as TREO hereafter) is a modular system designed to treat abdominal aortic and aorto-iliac aneurysms. The TREO consists of four types of implants, specifically a Main Bifurcated Stent-Graft, a Leg Extension Stent-Graft, a Proximal Cuff Stent-Graft and a Straight Iliac Extension Stent-Graft.

Each patient receives at least a TREO Main Bifurcated Stent-Graft and two Leg Extension Stent-Grafts (see **Figure 1**), each delivered via an endovascular approach using their own separate delivery system. Patients may also receive Proximal Cuff Stent-Grafts and Straight Iliac Extension Stent-Grafts. All stent-grafts are comprised of self-expanding Nitinol stents sutured to woven polyester fabric. The stent scaffold is a series of sinusoidal springs stacked in a tubular configuration. These stents are spaced along the length of the graft fabric to provide radial support and allow for the self-expansion of the stent-grafts. Radiopaque markers are placed on the stent-graft to aid visualization and accurate placement.

Stent-grafts

The Main Bifurcated Stent-Graft has an uncovered proximal stent that includes fixation barbs (suprarenal) for migration resistance. A second row of barbs are also located distally to the start of the covered section, approximately at the middle of the first covered stent, to help provide infrarenal fixation. Each gate of the Main Bifurcated Stent-Graft is designed to accept a Leg Extension Stent-Graft. The diameter of each gate of the Main Bifurcated Stent-Graft is always the same size (14 mm), regardless of proximal diameter or length. Each leg gate of the Main Bifurcated Stent-Graft also includes a Nitinol lock stent that is sewn on the inside of the graft fabric. The lock stent contains dull barbs that are intended to engage the Leg Extension Stent-Graft *in-situ* and help prevent separation of the Leg Extension Stent-Graft from the Main Bifurcated Stent-Graft.

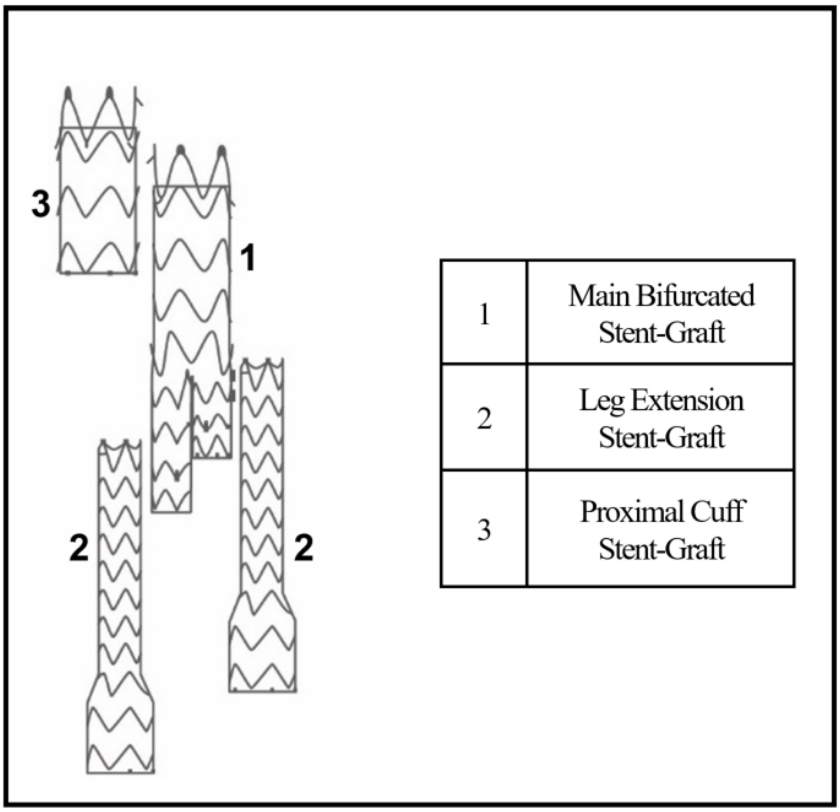
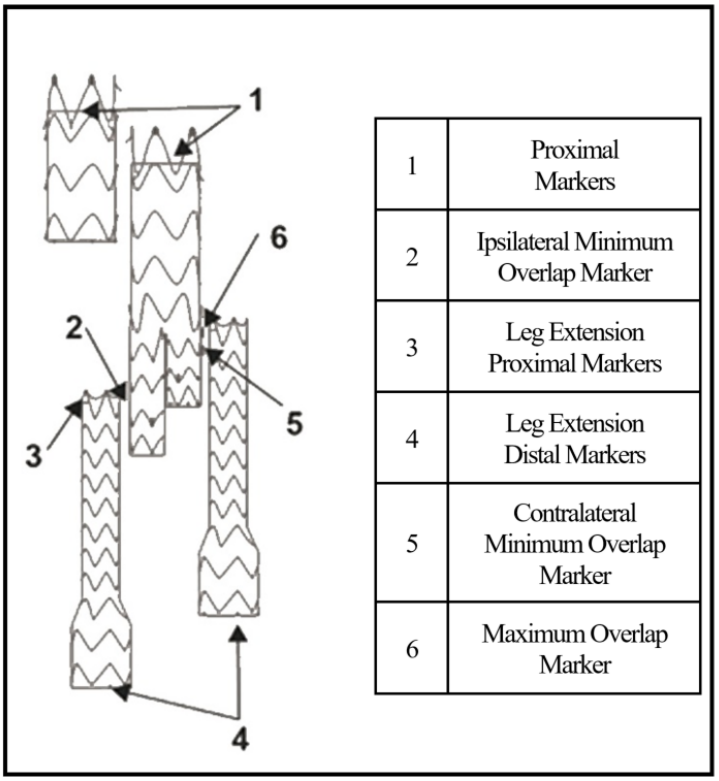


Figure 1. TREO® Abdominal Stent-Graft Components

The proximal end of all Leg Extension Stent-Grafts is always of the same diameter (15 mm) to allow coupling with any Main Bifurcated Stent-Graft. In addition, the amount that each Leg Extension Stent-Graft is inserted into the gate of the Main Bifurcated Stent-Graft is adjustable.

Additional ancillary endovascular stent-grafts are also available. Proximal Cuff Stent-Grafts are available for all Main Bifurcated Stent-Grafts if proximal extension is needed. The proximal end of the Proximal Extensions (Cuff Stent-Grafts) is configured identically to the proximal ends of the Main Bifurcated Stent-Grafts.

Radiopaque markers are sewn onto all stent-grafts to aid in the visualization and placement of the device. The markers are made of a platinum iridium alloy that is 90% Platinum and 10% Iridium. The suture that is used to attach the marker bands is the same as that used for the stents. Radiopaque markers are identified in **Figure 2**.



1	Proximal Markers
2	Ipsilateral Minimum Overlap Marker
3	Leg Extension Proximal Markers
4	Leg Extension Distal Markers
5	Contralateral Minimum Overlap Marker
6	Maximum Overlap Marker

Figure 2. Minimum Overlap Markers

The bare stent and lock stent of the TREO stent-grafts are produced from laser cut Nitinol tubing while all of the remaining Nitinol components used in the device are produced from shape-set Nitinol wire.

Product Size Availability

The TREO® Abdominal Stent-Graft System is intended to be used as a three-piece modular system consisting of a Main Bifurcated Stent-Graft and two Leg Extension Stent-Grafts. Each stent-graft is available as follows:

- The Main Body Bifurcated Stent-Grafts are available in proximal diameters ranging from 20 mm to 30 mm in 2 mm increments, 33 mm, and 36 mm with the corresponding vessel size requirement. Each proximal diameter is available in 3 body lengths.
- Each leg gate of the Main Bifurcated Stent-Graft is always the same diameter (14 mm), regardless of the proximal diameter size. This allows using any Leg Extension Stent-Graft with any Main Body Bifurcated Stent-Graft.
- The proximal diameter of every Leg Extension Stent-Graft is always 15 mm. Leg Extension Stent-Grafts are available in distal diameters of 9, 11, 13, 15, 17, 20, and 24 mm. Available lengths range from 80 mm to 160 mm.
- The Proximal Cuff Extensions are available in proximal diameters ranging from 20 mm to 30 mm in 2 mm increments, 33 mm, and 36 mm. Each is available in 3 body lengths of 40 mm, 55 mm, and 70 mm.

- Straight Extensions are available in diameters of 9, 11 and 13 mm. The proximal and distal diameters are the uniform along the length of each Straight Extension Stent-Graft. Straight Extension Stent-Grafts come in one length of 80 mm. Straight Extension Stent-Grafts are only intended for extending a previously placed Leg Extension Stent-Graft that has an identical distal diameter. Straight Extensions are not intended for use directly with a Main Bifurcated Stent-Graft.

Delivery Systems

The TREO Main Bifurcated Stent-Graft and Proximal Cuff Stent-Graft use the same delivery system, consisting of an introducer sheath attached to a main handle assembly. The handle assembly includes a Black Stationary Grip and Gray Turn Knob control system for accurate placement of the Main Bifurcated or Proximal Cuff Stent-Graft.

The introducer sheath and tip are hydrophilically coated. The sheath can be detached from the handle assembly and left in place while removing the rest of the delivery system, so the introducer sheath can then be used as a vascular introducer for the ipsilateral Leg Extension Stent-Graft and/or other devices. The tip of the delivery system and end of the introducer sheath are radiopaque for visibility during use. The delivery systems profiles are 18Fr or 19Fr depending on the proximal diameter of the Main Bifurcated or Proximal Cuff Stent-Graft. See **Figure 3** below.

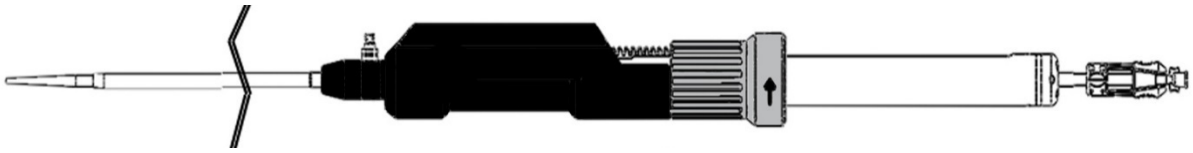


Figure 3. TREO Main Body and Cuff Delivery System

The TREO Leg Extension and Straight Extension Stent-Grafts use a similar version of the Delivery System as the Main Bifurcated and Proximal Cuff Stent-Grafts. The differences between the Delivery System for the Leg Extension and Straight Extensions and the Main Bifurcate and Proximal Cuff delivery systems are the absence of the clasp release mechanism at the proximal end of the delivery system next to the guidewire flush port, sheath and tip diameter, and usable length. The delivery systems profiles are 13Fr or 14Fr. depending on the distal diameter of the Leg Extension or Straight Extension Stent-Graft. See **Figure 4** below.

Figure 4. TREO Leg Extension and Straight Extension Stent-Graft Delivery System

Additional details can be found in the TREO® Abdominal Stent-Graft System Instructions for Use.

VI. ALTERNATIVE PRACTICES AND PROCEDURES

There are several other alternatives for the treatment of infrarenal abdominal aortic and aorto-iliac aneurysms, including endovascular repair using other endovascular grafts, medical management, and 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

The TREO® Abdominal Stent-Graft System is commercially available within the European Union (Austria, Belgium, Bulgaria, Czech Republic, Denmark, France, Germany, Greece, Hungary, Ireland, Italy, Netherlands, Poland, Portugal, Romania, Slovakia, Spain, Sweden). In addition, TREO is commercially available Argentina, Brazil, Chile, Hong Kong, Israel, Jordan, Lebanon, Norway, Palestine, Singapore, South Africa, Switzerland, Thailand, Uruguay and Vietnam.

TREO 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 use of the device:

Table 1. Potential Adverse Events

Amputation	Hemorrhage
Anesthetic reactions/complications (e.g., aspiration)	Hepatic failure
Aneurysm Sac Enlargement	Impotence
Aneurysm / Lesion Rupture	Infection
Aortic damage (perforation, dissection, bleeding, rupture)	Ischemia (spinal cord, perfusion pathways)
Arteriovenous fistula / aorto-duodenal fistula	Limb ischemia
Blood Loss	Open surgical conversion
Bowel complications (e.g., adynamic ileus, transient ischemia, infarction, necrosis)	Paralysis/Paresthesia/Paraparesis
Cardiac events (e.g., arrhythmia, congestive heart failure, myocardial infarction, hypotension, hypertension)	Post Implantation Syndrome
Cerebral vascular accident (stroke)	Pseudoaneurysm

Table 1. Potential Adverse Events	
Claudication (e.g., buttock, lower limb)	Radiation overexposure or reaction
Coagulopathy	Renal failure or Complications
Contrast toxicity / anaphylaxis	Stenosis of native vessel
Death	Stent fracture / break
Delivery system failure	Stent-Graft failure (e.g., improper component placement, graft material wear, suture break, dilatation, erosion, graft twisting or kinking, puncture, perigraft flow)
Deployment failure (partial or inaccurate deployment)	Stent-Graft migration
Embolism (micro and macro) with transient or permanent ischemia or infarction	Transient Ischemic Attack
Endoleak	Vascular Trauma (perforation / dissection)
Fever and localized inflammation	Vessel Damage
Gastrointestinal complications	Vessel Dissection
Genitourinary complications (e.g., ischemia, erosion, femoral-femoral artery thrombosis, fistula, incontinence, hematuria, infection)	Vessel Occlusion/Thrombosis
Hematoma (surgical)	Wound complications (dehiscence, infection, hematoma, seroma, cellulitis)

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

IX. SUMMARY OF NONCLINICAL STUDIES

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

A. Laboratory Studies

TREO underwent testing for design verification and validation, including long-term durability and corrosion testing. Testing was performed in accordance with ISO 25539-1:2017, *"Cardiovascular implants – Endovascular devices – Part 1: Endovascular prostheses"* and ISO 25539-1:2003/A1, *"Cardiovascular implants – Endovascular devices – Part 1: Endovascular prostheses, Amendment 1: Test Methods."* For the evaluation of TREO, a subset of device components and sizes were used for each test or alternatively, the worst-case configuration/size was selected. This sample selection represented the full size range available for TREO. A summary of this testing is provided in **Table 2** and **Table 3**.

Asterisk (*) indicates that the testing was performed at baseline and after aging (accelerated or real time to the shelf life duration).

Table 2. Non-Clinical Testing: Delivery System

Test Name	Test Purpose	Acceptance Criteria	Results
Dimensional verification of the endovascular system*	To evaluate the conformance of the TREO's dimensions to their design specifications, and to evaluate the compatibility of the TREO with its accessory devices listed in the IFU. Also, to determine the TREO's maximum diameter at the loaded stent-graft section (largest profile) in order to evaluate the dimensional compatibility between the aged delivery system and the vasculature.	System must be compatible with 0.035" guidewire and 0.036" mandrel.	Pass
		Delivery system sheath outer diameter (O.D.) must meet pre-determined tolerances. - 14Fr = 0.183" ±0.002" (4.65mm ± .05mm) - 13Fr = 0.170" ±0.002" (4.32mm ± .05mm) - 18Fr = 0.239" ±0.002" (6.07mm ± .05mm) - 19Fr = 0.252" ±0.002" (6.40mm ± .05mm)	Pass
		All test samples must meet the nominal labeled profile.	Pass
		Useable length: – Main Body = 52.2 cm ± 1.6 cm – Leg System = 84.2 cm ± 0.5cm	Pass
Simulated Use (Including Force to Deploy)*	An overall assessment of the TREO was conducted during which qualitative assessments are made as well as quantitative measurements. The TREO was prepared, deployed and the delivery system is then removed from an anatomical model. The anatomical model was designed to challenge both access as well as implant site requirements. Assessments included: • Ability to prepare system. • Ability to track system to landing zone, while ensuring direct assessment of attributes such as kink resistance, pushability and torquability. • Forces required to deploy system at each step, including the stent-graft as well as the proximal clasp, if applicable. • Ability to accurately deploy the stent-graft at the target landing zone. • Ability to successfully withdraw the delivery system. Other assessments included: sheath stretching, stent-graft twisting, ability to re-position the device prior to final deployment, tip re-seating, insertion of leg device into main sheath (if applicable) and valve hemostasis.	Bifurcated & Cuff Graft Deployment Force: < 45lbs. (200.2N)	Pass
		Leg Graft Deployment Force: ≤ 38lbs	Pass
		Clasp Release: ≤ 10lbs. (44.5 N)	Pass
		Leg Clasp Release from sheath: ≤ 10lbs. (44.5 N)	Pass
		All qualitative assessments must meet acceptance criteria: • System must be able to be prepped with saline passing through guidewire lumen and out the distal end of the sheath. • Device must successfully track to deployment site while assessing for the ability to torque the device. • Device must not kink prior to or during deployment. • Device must deploy at designated landing zone. • Delivery system must be withdrawn without catching on deployed stent-graft. • Sheath hemostasis valve must not leak > 15cc in one minute.	Pass

Table 2. Non-Clinical Testing: Delivery System

Test Name	Test Purpose	Acceptance Criteria	Results
Tensile Bond Strength*	To determine the bond strength of the joints and/or fixed connections of the TREO.	Sub-assemblies tested must meet pre-determined pull forces depending on the bond or tubing requirements. Acceptance criteria ranged from 5 lbs to 50 lbs (22.2 N to 222.4N).	Pass
Torsional Bond Strength	To determine the torque required to cause failure of the bonded joints of the TREO.	The delivery system sheath introducer must be torqued at 180 degrees without any damage to the sheath bond.	Pass
Hemostasis*	To evaluate the TREO's ability of any seals or valves to maintain adequate hemostasis for the Bifurcated and Leg system.	Amount of water obtained through leaking in 1 minute should be < 15 cc.	Pass
Lubricity Test	To determine the lubricity of the hydrophilically coated Tip and Introducer Sheath.	The force must meet the current specification for acceptable lubricity tests with 95/90 confidence/reliability: - Sheath Spec: = 400g (3.9N) - Tip Spec: = 800g (7.8N)	Pass

Table 3. Non-Clinical Testing: Implant

Test Name	Test Purpose	Acceptance Criteria	Results
MR Compatibility	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 TREO is MR Conditional. A person with this device can be safely scanned in an MR system meeting the following conditions: • Static magnetic field of 1.5-Tesla and 3-Tesla • Maximum spatial gradient magnetic field of 4,000-Gauss/cm (40 T/m) or less • Maximum MR system reported, whole body averaged specific absorption rate (SAR) of 4-W/kg (First Level Controlled Operating Mode)	Pass
Leakage at Seal Zone	To determine if the fixation points are against the mock artery completely in order to address the sealing characteristics.	Lack of voids in contact between the stent-graft and model wall.	Pass

Table 3. Non-Clinical Testing: Implant

Test Name	Test Purpose	Acceptance Criteria	Results
Migration Resistance	To determine the force required to displace the stent-graft in a mock artery. This test provided an indication of the resistance to migration provided by the fixation mechanisms of the stent-graft.	Migration Specification: ≥ 25N	Pass
Separation Force for Overlapping Endovascular Prostheses	To determine the force required to separate the modular components of the stent-graft or to separate overlapping stent-grafts in the deployed state	Modular junction force: ≥ 4N	Pass
Compression Resistance Flat Plate Full Length Crush Resistance	To determine the force required to cause buckling and permanently radially deform or fully collapse the stent-graft and to determine if it recovers to its original geometry after testing.	Observations were documented as pass/fail. If any permanent deformation occurred to the stent-graft, the test was considered a failure. The force used to crush the stent-graft at 50% diameter and full collapse as well as the deflection was recorded.	Pass
Compression Resistance Local Compression	To determine the deformation of the stent-graft in response to a localized compressive force, perpendicularly applied to the longitudinal axis of the stent-graft, and to determine if it recovered to its original geometry after testing.	Observations were documented as pass/fail along with the forces used to compress the stent-graft and the deflection observed. Any deformation to the stent-graft was considered a failure.	Pass
Radial Force (Self-Expanding Endovascular Prostheses)*	To determine the force exerted by a self-expanding implant as a function of the implant diameter.	Positive radial load.	Pass
Resistance to Kinking (Flexibility)	To determine the minimum radius of curvature that the stent-graft can accommodate without kinking and if it can recover to its original geometry.	The stent-graft must bend into various radii without kinking, and/or permanent deformation. Kinking is defined as a reduction in lumen area of greater than approximately 50%. Additionally, the stent-graft must return to its original geometry.	Pass
Integral Water Leakage	To determine the rate of water leakage through the entire stent-graft, incorporating all modular components and extension devices.	Stent-graft leakage: < 168 ml / min / cm^2	Pass
Water Permeability (Textile Materials)	To determine the rate of fluid flow through the wall of the stent-graft as virgin material.	Textile Component Native Permeability: < 120 ml / min / cm^2	Pass

Table 3. Non-Clinical Testing: Implant

Test Name	Test Purpose	Acceptance Criteria	Results
Dimensional Verification of the Endovascular Prosthesis	To determine the relationship between the AAA stent-graft length and diameter following deployment in order to assess foreshortening.	The length of the stent-graft must be within specification while compressed in the minimum and maximum simulated vessel sized tubes	
		Length = (± 2mm) for Bifurcated and Leg Extension Stent-grafts	Pass
		Length= (± 1mm) for Cuff Stent-grafts	Pass
	To determine the outer diameter of the TREO stent-grafts in the deployed state for verification to design specifications. The purpose of this test is to show that the implant can withstand the strains experienced in radial compression during loading / unloading without any significant change to its dimensions or geometry.	Relaxed outer diameter post deployment	
		Outer diameter for cuffs, bifurcates and legs 17mm and larger must be within -1mm / +2mm of the nominal diameter at the proximal, middle and distal ends.	Pass
		Outer diameter must be within 0mm / +2mm for 8mm – 15mm legs.	Pass
Burst Strength*	To determine the pressurized burst strength or circumferential strength of the stent-graft if used with an accessory balloon.	The stent-graft must withstand 1.5 ATM of pressure without damage.	Pass
Longitudinal Tensile Strength (Stent-Graft)*	To determine the longitudinal tensile strength of the stent-graft.	Textile Component Native Tensile Force: ≥ 150 lbf	Pass
Strength of the Connection(s) or Bond(s) Between the Graft material and the stent(s) or attachment system(s)	To determine the strength of the fixation between the graft material and the stent/attachment system.	≥ 48.5 lbs (215.7 N) for a composite pull test of 5 apexes.	Pass
Visibility	To evaluate the ability to visualize the TREO using the imaging techniques specified in the IFU.	Test units must be visible under fluoroscopy.	Pass
Corrosion	To evaluate the corrosion resistance properties of the TREO's (all Nitinol) metallic components.	All samples display breakdown potentials equivalent or better to a comparison device.	Pass
Fatigue and Durability — Computational Analyses	Finite element analysis (FEA) was used to compute the maximum strains in all of the TREO design's sizes when subjected to catheter loading and an in-vivo pulsatile loading environment.	Characterization study. The worst-case component size was identified and used to inform the selection of the worst-case prosthesis size for *in vitro* fatigue testing.	Pass

Table 3. Non-Clinical Testing: Implant

Test Name	Test Purpose	Acceptance Criteria	Results
Fatigue and durability — *In-vitro* testing	Pulsatile Fatigue Testing: To evaluate the long-term durability of the stent-graft design over 380 million cycles of pulsatile fatigue loading.	The samples must not exhibit physical damage that would represent a failure of their safety or function due to: 1. Component deformation, separation or fractures leading to ineffective proximal or distal seals, migration or severed pieces into the bloodstream 2. Fabric holes larger than 0.5 mm^2 3. Modular disjunctions 4. Compromised luminal integrity due to twisting or component collapse All anomalies must be studied on a case-by-case basis. Anomalies due to test artifacts will not be representative of failure in safety or function of the design.	Pass
	Pulsatile Bending Testing: To evaluate the long-term durability of the stent-graft design over 380 million cycles of bending loads.		Pass
	Axial Fatigue Tests: To evaluate the long-term durability of TREO's bare proximal stent engagement features and the limbs' modular junction engagement features for 380 million cycles.	The samples must not exhibit physical damage that would represent a failure of their safety or function due to: 1. Component deformation, separation or fractures leading to ineffective proximal seals, migration or severed pieces into the bloodstream 2. Fabric holes larger than 0.5 mm^2 3. Modular disjunctions	Pass

Fracture Root Cause Investigation

As described below, the TREO was evaluated in a clinical study. During the clinical study, bare proximal stent fractures were observed in three areas of the component: the suprarenal barb, the proximal end of a stent strut, and the distal end of a stent strut (for detailed description, see Section X.D.2.2.8 Stent-Graft Integrity). A root cause analysis and evaluation of the potential impact on device performance was conducted that evaluated materials and components, manufacturing processes, clinical procedure, patient anatomical data, bench top performance testing of fractured test samples, biomechanical analysis, computational modeling, and experimental fatigue testing.

Root Cause Investigation

Biomechanical analyses of TREO patients identified axial deformation and barb flexion occurring during aortic pulsation. Subsequent computational modeling predicted that axial drag forces from blood flow and barb penetration depth are primary factors impacting fatigue fracture at the suprarenal barbs and struts of the bare proximal stent.

Experimental fatigue testing was conducted to investigate the learnings from the biomechanical analysis and computational modeling.

Accelerated axial fatigue testing (intended to represent 10 years of physiologic loading) of the bare proximal stent resulted in fractures of the cranial barbs and a strut, which were consistent with the fracture locations and rates reported in the clinical study.

Fatigue-to-fracture testing was also conducted to further characterize the effect of axial loading on device fracture. The test results predicted barb penetration as an important consideration in component fracture. From a mechanics perspective, minimal barb penetration results in a larger bending moment and increased loading on the component. Minimal barb penetration can manifest clinically in patients with less oversizing. Clinical analysis of the study subjects showed that devices with strut fracture tended to be less oversized; however, similarly oversized devices were also not associated with fracture observations. Due to the low sample size of patients with fracture as compared to the overall study sample size, and that patients with devices with similarly less oversizing did not exhibit fractures, no definitive relationship between oversizing and fracture could be confirmed.

In summary, the root cause evaluation identified axial drag forces from blood flow and minimal barb penetration as potential contributing causes of bare proximal stent fracture. The information from the root cause investigation did not identify patient anatomical, demographic, or procedural related factors that may contribute to an increased risk of fracture.

Evaluation of Potential Impact of Stent Fracture on Device Performance

It was identified that two critical device performance characteristics that may be affected by stent fracture and result in clinical sequelae were stent-graft displacement (migration) resistance and radial force. Comparative testing was conducted to characterize the following conditions:

- "Intended" condition – Test samples with no fractures, representing the control.

- "Beyond-fault" condition – Test samples that consisted of device fracture conditions of multiple stent strut or barb fractures that exceeded the observations from the clinical study (two study subjects had multiple stent fractures of: 4 stent strut fractures in a single device; and 2 barb fractures in a single device). The intent of this testing was to characterize the impact of stent fractures on device performance and the number of fractures that may significantly decrease the device's ability to provide its intended function.

With the exception of test samples with 4 fractured barbs (exceeding the observations from the durability bench testing and the clinical study), all other device conditions met the same pre-defined acceptance criteria for design verification and validation testing of migration resistance and radial force as listed in **Table 3.** The results support that with respect to the bare proximal stent fractures observed in the durability bench testing and clinical study, fractured TREO devices are expected to still meet their performance requirements in a controlled benchtop setting.

B. Animal Studies

In-vivo animal study testing (acute and chronic) was conducted on the TREO® Abdominal Stent-Graft System.

- The acute study consisted of 2 animals and was designed to evaluate the intra-operative features of delivery and hemostasis of the TREO® Stent-Graft System. The test articles in the acute study consisted of 14 mm stent-grafts representative of the distal section of the TREO Bifurcated Stent-Graft and 15.3 mm stent-grafts representing the proximal section of the TREO Leg Extension Stent-Graft.

- The chronic study consisted of 21 animals with the objective of evaluating the safety of the device following implantation in ovine aorta and iliac arteries at 6 weeks (7 sheep), 12 weeks (6 sheep) and 26 weeks (8 sheep). The test articles in the chronic study consisted of 14 mm stent-grafts representative of the distal section of the TREO Bifurcated Stent-Graft and 15.3 mm stent-grafts representing the proximal section of the TREO Leg Extension Stent-Graft and 20 mm Main Bifurcated surrogates similar to the Proximal Cuff design. The 20 mm device was placed in an appropriately sized area of the abdominal aorta alone. The 14 mm device was placed in an appropriately sized portion of the abdominal aorta distal to the 20 mm device and then the 15.3 mm device was placed inside of the deployed 14 mm device. The tissue response to TREO was evaluated histologically, and the sealing capability and integrity of the stent-graft were evaluated angiographically and radiographically, respectively.

The results of both the chronic and acute study supported that the TREO is well-tolerated in the ovine model and does not adversely affect the general health of animals. The acute study results support that the TREO can be accurately deployed in the aorta. The results of the chronic animal study showed that the device was successfully deployed, remained intact and patent through study duration, and had appropriate tissue response.

There was no device-related mortality and no evidence of adverse systemic effects in either the acute or chronic animal studies.

See **Table 4** below for results of the animal studies.

Table 4. Results of Animal Studies

Study	# of Animals	Objectives	Results
GLP Acute Performance Assessment of the Bolton Medical Aortic	2	To evaluate the acute performance of the modified TREO to verify the accuracy of deployment, visibility of the device under fluoroscopy,	The Main Bifurcated Stent-Graft, Leg Extension Stent-Grafts and their respective delivery systems were graded

Table 4. Results of Animal Studies

Study	# of Animals	Objectives	Results
Stent Graft in Ovine Model		and hemostasis of the sheath valve.	above average overall. Accuracy of deployment of the Leg Extension Stent-Graft was satisfactory. The radiopacity of the Main Bifurcated and Leg Extension Stent-Grafts was confirmed, and the device was visible under fluoroscopy. Blood loss through the closed hemostasis valves of the Main Bifurcated and Leg Extension delivery systems was absent or miniscule and, in most cases, minimal with the valve open. Radiographs of the explanted Main Bifurcated and Leg Extension Stent-Grafts showed the stents were accurately overlapped. The explanted stent pairs were engaged and remained intact when tensile testing was performed.
Chronic Evaluation of a Stent-Graft in an Ovine mode	21	To evaluate the delivery/ deployment associated with the TREO when placed in the thoracic or abdominal aorta and/or iliac artery position, through the femoral artery.	All devices were deployed, and no device-related adverse events occurred during deployment and subsequent recovery.

Table 4. Results of Animal Studies

Study	# of Animals	Objectives	Results
		To evaluate the physiological function (e.g., patency, integrity) associated with the TREO when placed in the thoracic or abdominal aorta and/or iliac artery position, through the femoral artery.	Histologic evaluation confirmed the fabric of the device remained intact at all time points and complete tissue incorporation of the fabric was observed at all time points for all devices.
		To evaluate the potential for thrombus associated with the TREO when placed in the thoracic or abdominal aorta and/or iliac artery position, through the femoral artery.	Histologic evaluation confirmed the presence of a complete anti-thrombogenic cell lining on the luminal surface of all devices.
		To evaluate the healing associated with the TREO when placed in the thoracic or abdominal aorta and/or iliac artery position, through the femoral artery.	Tissue analysis indicated no evidence of necrosis and minimal inflammatory response.

C. Biocompatibility

The biocompatibility assessment performed on TREO was based on the matrix for body contact and contact duration as specified in ISO 10993-1:2009/(R)2013, "*Biological evaluation of medical devices – Part 1: Evaluation and testing within a risk management process.*" The TREO is comprised of an implantable stent-graft and a corresponding delivery system. For purposes of the biocompatibility assessment, the stent-graft was classified as an implant device, permanent contact (> 30 days), while the delivery system was classified as an external communicating device, circulating blood, limited exposure (< 24 hours). All testing was conducted by a qualified contract laboratory in accordance with FDA GLP regulations, 21 CFR 58.

All testing performed met the pre-specified acceptance criteria. The results are results are summarized in **Table 5** for the Implant and **Table 6** for the delivery system.

Table 5. Biocompatibility Evaluation - TREO Implant

Biological Effect (Test)	Purpose	Results	Acceptance Criteria Met?
ISO MEM Elution Cytotoxicity	To determine if stent-graft extracts cause cytotoxicity when exposed to L-929 fibroblast cells.	Non-cytotoxic: Grade 2 (mild reactivity).	Yes

Table 5. Biocompatibility Evaluation - TREO Implant

Biological Effect (Test)	Purpose	Results	Acceptance Criteria Met?
ISO Guinea Pig Maximization Sensitization	To evaluate the allergenic/sensitization potential of stent-graft extracts in guinea pigs.	Non-sensitizer: All animals scored 0 resulting in 0% sensitization rate.	Yes
ISO Intracutaneous Reactivity	To evaluate stent-graft extracts for potential irritation effects after intracutaneous injection in rabbits.	Non-irritant: The difference between the test article extracts overall mean score and corresponding control overall mean score was less than 1.0.	Yes
ISO Acute Systemic Toxicity	To evaluate stent-graft extracts for potential toxic effects after single-dose systemic injections in mice.	There was no mortality or evidence of systemic toxicity from the test article extracts.	Yes
Material Mediated Pyrogenicity	To evaluate the stent-graft for the potential of inducing a pyrogenic response in rabbits.	Non-pyrogenic: rabbits showed a maximum temperature rise of 0.0, 0.1, and 0.2°C, respectively over the 3 hour test period.	Yes
Genotoxicity /Mutagenicity			
• Ames Assay	To evaluate the mutagenic potential of the stent-graft by measuring its ability to induce back mutations at selected loci of several strains of bacteria.	Non-mutagenic: The stent-graft did not cause an increase in point mutations, exchanges or deletions.	Yes
• *In vitro* Mouse Lymphoma	To evaluate the potential of the stent-graft extracts to induce a forward mutation in the TK locus of L5178Y TK+/- cells.	The stent-graft is considered to be non-mutagenic in the test system.	Yes
• *In-vivo* Mouse Micronucleus	To evaluate the potential of the stent-graft to induce *in-vivo* clastogenic events or damage to the mitotic spindle in polychromatic erythrocytes obtained from mouse bone marrow.	The stent-graft is considered to be non-mutagenic in the test system.	Yes
Hemocompatibility			
• Hemolysis	To evaluate the potential of the stent-graft to cause hemolysis in direct contact or by extraction.	Non-hemolytic: Percent hemolysis: Direct contact – 0.6% Extract – 0.0%	Yes
• Partial Thromboplastin Time (PTT)	To determine the potential of the stent-graft to cause an effect on the coagulation cascade via the intrinsic coagulation pathway.	Minimal activator of intrinsic coagulation pathway: The stent-graft had an average clotting time of 256.9 seconds (86% of the negative control).	Yes

Table 5. Biocompatibility Evaluation - TREO Implant

Biological Effect (Test)	Purpose	Results	Acceptance Criteria Met?
• Complement Activation	To determine the potential of the stent-graft to activate complement.	C3a – potential activator of the complement system SC5b-9 – not considered to be a potential activator of the complement system	Yes
Rabbit Intramuscular Implant			
• 4 weeks	To evaluate the potential for local and systemic toxic effects of a test article in direct contact with skeletal muscle of the rabbit for 4 weeks.	The macroscopic reaction was not significant as compared to the negative control implant material. Microscopically, the test article was classified as a slight irritant as compared to the negative control article.	Yes
• 12 weeks	To evaluate the potential for local and systemic toxic effects of a test article in direct contact with skeletal muscle of the rabbit for 12 weeks.	The macroscopic reaction was not significant as compared to the negative control implant material. Microscopically, the test article was classified as a moderate irritant as compared to the negative control article.	Yes
• *In-vivo* thrombogenicity *	N/A *	N/A *	
Chemical Characterization	To assess the exhaustive extractables profile of the stent-graft.	Based on the available toxicity data, exposure estimates, and safety margins, the likelihood of extractable chemicals from the stent-graft producing unacceptable carcinogenic or non-carcinogenic health risks in the adult patient population under the proposed conditions and duration of clinical use (permanent; >30 days) is acceptable.	Yes
***In-vivo* thrombogenicity of the stent prosthesis was assessed at 6, 12 and 26 weeks as part of the *in-vivo* safety study summarized in Section IX (B).			

Table 6. Biocompatibility Evaluation - TREO Delivery System

Biological Effect (Test)	Purpose	Results	Acceptance Criteria Met?
ISO MEM Elution Cytotoxicity	To determine if delivery system extracts cause cytotoxicity when exposed to L-929 mammalian cells.	Non-cytotoxic: Grade 0	Yes
ISO Guinea Pig Maximization Sensitization	To evaluate the allergenic/sensitization potential of delivery system extracts in guinea pigs.	The test article did not elicit a sensitization response.	Yes
ISO Intracutaneous Reactivity	To determine if any chemicals that may leach or be extracted from the test article were capable of causing local irritation in the dermal tissues of rabbits.	Non-irritant: The difference between the test article extracts overall mean score and corresponding control overall mean score was less than 1.0.	Yes
ISO Acute Systemic Toxicity	To evaluate delivery system extracts for potential toxic effects after single-dose systemic injections in mice.	There was no evidence of systemic toxicity from the test article extracts.	Yes
Material Mediated Pyrogenicity	To evaluate the delivery system for the potential of inducing a pyrogenic response in rabbits.	Non-pyrogenic: rabbits showed a maximum temperature rise of 0.0, 0.2, and 0.3°C, respectively over the 3 hour test period.	Yes
Genotoxicity /Mutagenicity			
• Ames Assay	To evaluate the mutagenic potential of the delivery system by measuring its ability to induce back mutations at selected loci of several strains of bacteria.	Non-mutagenic: The stent-graft did not cause an increase in point mutations, exchanges or deletions.	Yes
• *In vitro* Mouse Lymphoma	To evaluate the potential of the delivery system extracts to induce a forward mutation in the TK gene of L5178Y TK+/- cells.	Non-genotoxic and non-mutagenic: Mutant frequencies and cloning efficiencies of preparations treated with stent-graft were within the limits defined for a negative response.	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 – 0.0% Extract – 0.0%	Yes
• Partial Thromboplastin Time (PTT)	To determine the time citrated plasma exposed to delivery system takes to form a clot when exposed to a suspension of phospholipid particles and calcium chloride.	The test article results are comparable to the reference control article results and the comparison control article results.	Yes

Table 6. Biocompatibility Evaluation - TREO Delivery System

Biological Effect (Test)	Purpose	Results	Acceptance Criteria Met?
• Platelet and Leukocyte count	To determine if the delivery system exposed to human whole blood in vitro would adversely affect the platelet and leukocyte ratios in whole blood.	The platelet and leukocyte counts of the test article sample were comparable to the reference and comparison controls.	Yes
• *In-vivo* thrombogenicity	To evaluate the potential of the test device to resist thrombus formation when placed in the vasculature.	No thrombus was observed on the delivery device.	Yes

D. Sterilization, Packaging and Shelf-Life

TREO is sterilized via gamma irradiation resulting in a sterility assurance level (SAL) of 10^{-6}. The production dose of 25 kGy is supported by a validation study that was executed in accordance with ISO 11137-2.

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 Terumo Aortic procedures. The TREO 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 2 and 3**. Accelerated and real time shelf-life product testing conducted on the TREO supports a 2-year shelf-life claim for the Main Bifurcated Stent-Grafts, the Proximal Cuff and the Straight Extension Stent-Grafts and a 3 year shelf life for the Leg Extension Stent-Grafts.

X. SUMMARY OF PRIMARY CLINICAL STUDY

The applicant performed a clinical study to establish a reasonable assurance of safety and effectiveness of endovascular repair of infrarenal abdominal aortic and aorto-iliac aneurysms with the TREO in the US under IDE #G100200. 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 November 25, 2013 and February 10, 2016. The database for this PMA reflected data collected through February 14, 2019 and included 150 patients. There were 29 US investigational sites.

The study was a multi-center, prospective, single-arm, non-randomized, non-blinded clinical study.

The primary safety endpoint was defined as the proportion of patients with a major adverse event (MAE) at 30 days post-procedure. The results were tested against a performance goal of 19%, derived from published data on open surgical controls.

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

Null hypothesis (H_0): $p_{saf} \geq 0.19$
Alternative hypothesis (H_1): $p_{saf} < 0.19$,

where p_{saf} was the proportion of patients with at least one major adverse event through 30 days post implant procedure.

The proportion of patients in the safety sample with composite MAE at 30 days post procedure was summarized as a number, percentage and an exact 95% confidence interval (Clopper-Pearson method). The probability of experiencing at least one MAE in the 30 days post procedure was tested versus the performance goal for the endpoint using an exact binomial test. In addition, the probability of experiencing at least one MAE in the 30 days post procedure was estimated using Kaplan-Meier method. Time to MAE was calculated by determining the number of days between the date of the procedure and the date of the first MAE. Patients without events (within the first 30 days post procedure) were censored at 30 days (for the primary safety analysis). Patients who withdrew from the study after device implantation were censored at the time of early discontinuation (if it occurred prior to 30 days).

The primary effectiveness endpoint was defined as the proportion of patients with successful aneurysm treatment after use of TREO through 1-year post implant procedure. The results were tested against a performance goal of 88%, derived from the clinical study data of commercially available endovascular grafts.

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

Null hypothesis (H_0): $p_{eff} \leq 0.88$
Alternative hypothesis (H_1): $p_{eff} > 0.88$,

where p_{eff} was the proportion of TREO patients with successful aneurysm treatment at 12 months post implant procedure.

The hypothesis of the primary safety endpoint was that the 30-day MAE rate in the Pivotal Study was lower than the performance goal of 19%. Assuming that the proportion of patients with at least one adverse event included in the definition of the composite MAE up to 30 days post-implant was 10.2%, 150 endovascular patients (receiving the TREO device) provided 80% power for an exact binomial test at a one-sided alpha level of 0.025 against the performance goal of 19%.

The hypothesis of the primary effectiveness endpoint was that the proportion of patients with the composite endpoint of successful aneurysm treatment at 12 months post-implant is at least 88% (estimated performance goal), and 127 endovascular patients (receiving TREO device and with 12 month follow-up) will provide better than 80% power for an exact binomial test at an one-sided alpha level of 0.025 against an alternative of 95.6% success rate. The goal of 127 patients with 12 months follow-up can be achieved with 150 enrolled patients assuming 15% attrition rate.

External evaluation groups were used during the course of the Pivotal Study, which are described below:

- *Independent Imaging Review Committee:* An independent imaging review committee, made up of a team of vascular surgeons, assessed each patient for anatomical approval for enrollment. This panel of physicians performed a concurrent review of the screening imaging after initial prescreening by the site. The investigators were ultimately responsible for considering both medical and anatomic criteria and determining patient's eligibility for the study based on the complete selection criteria.

- *Imaging Core Laboratory:* Following a patient's enrollment in the study, the Cleveland Clinic Peripheral Vascular Core Laboratory evaluated all imaging obtained during the course of the study. This review included confirmation of anatomical requirements for enrollment, along with assessment of follow-up imaging endpoints.

- *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 major adverse events reported by the site and classified them as related or not related to the device or the procedure. 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.

1. Clinical Inclusion and Exclusion Criteria

   Enrollment in the Pivotal Study was limited to patients who met the following inclusion criteria:

   - Age between 18 and 85
   - Infrarenal AAA with or without iliac artery involvement, with contrast CT performed within 4 months of planned implant procedure
   - Infrarenal AAA:

    - ≥ 4.5 cm in diameter for males, or ≥ 4.0 cm in diameter for females, or
    - increased in diameter by 0.5 cm in the last 6 months
- AAA anatomy including:
    - infrarenal landing neck length of 10mm or greater and an angle of less than 60 degrees relative to the long axis of the aneurysm (centerline at lowest renal to centerline at bifurcation) and a suprarenal neck angle of less than 45 degrees relative to the infrarenal neck axis and an outside diameter of 17mm – 32mm, or
    - infrarenal landing neck length of 15mm or greater and an angle of between 60 and 75 degrees relative to the long axis of the aneurysm and a suprarenal neck angle of less than 45 degrees relative to the infrarenal neck axis and an outside diameter of 16mm – 30mm
- Infrarenal landing neck meeting the vessel size requirements specified in the Instructions for Use (IFU) for the corresponding devices
- Lowest renal artery at least 9 cm from the aortic bifurcation
- Distal iliac landing neck with
    - an inside diameter of 8 mm – 13 mm and a length of at least 10 mm, or
    - an inside diameter of >13 mm – 20 mm and a length of at least 15 mm
- Distal iliac landing neck meeting the vessel size requirements specified for the corresponding devices in the IFU
- Total treatment length of at least 13 cm
- A distal aortic diameter above the iliac bifurcation ≥70% of the sum of the selected leg graft diameters that would pass through the same
- Patient was willing and able to comply with 1-month, 6-month, and 12-month follow-up visits, as well as annual visits out to 5 years
- Adequate renal function to tolerate required follow-up contrast enhanced CTs
- Adequate vascular access (e.g., patent iliac or femoral arteries) for introduction of the delivery system, which is 18F (6.0 mm) or 19F (6.3 mm) outer diameter, based on size of device used. Alternatively, patient's anatomy was suitable for creation of an iliac conduit
- Patient or Legally Authorized Representative agreed to sign Informed Consent Form

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

- Patient was pregnant or lactating
- Dissection in abdominal aorta, ruptured aneurysm, or symptomatic aneurysm (as determined by treating physician)
- Patient had a patent inferior mesenteric artery that could not be sacrificed and an occluded or stenotic celiac and/or superior mesenteric artery
- Implant procedure as planned did not allow for at least one patent hypogastric artery left intact, unless both were occluded on pre-op imaging

- Lesion that could not be crossed by a guide wire
- Proximal neck could not increase by more than 10% over 15mm or more than 7% over 10mm (i.e., no trapezoidal necks)
- Patient had severe untreated coronary artery disease and/or unstable angina, significant areas of myocardium at risk (based on coronary angiogram or radionuclide scans), left ventricular ejection fraction < 20%, or recent diagnosis of CHF
- Stroke or myocardial infarction within 6 months of the planned treatment date
- Patient had chronic obstructive pulmonary disease requiring routine need for oxygen therapy outside the hospital setting (e.g., daily or nightly home use)
- Patient had an active systemic infection or was suspected of having an active systemic infection (e.g., AIDS/HIV, sepsis)
- Morbidly obesity (more than 100% over the ideal body weight or as defined by institutional standards) or other clinical conditions that had the potential to severely compromise or impair x-ray visualization of the aorta
- Connective tissue disease (e.g., Marfan syndrome)
- Mycotic aneurysm
- Significant or circumferential calcification or mural thrombus in the proximal aortic neck or distal landing zone.
- Significant or circumferential calcification or mural thrombus within the treatment length, which could have adversely impacted device patency
- Patient had a blood coagulation disorder or bleeding diathesis, the treatment for which could not be suspended pre- and post-repair
- Patient was in acute or chronic renal failure (creatinine $\geq$ 2.5 mg/dL), unless patient was stable on dialysis
- Patient had less than two-year life expectancy as evidenced by factors prohibiting major medical intervention (e.g., presence of malignancy, severe cardiopulmonary disease)
- Patient was participating in another research study, had received investigational study drug within 30 days of planned procedure, or had received an investigational device within one year of planned procedure
- Patient was confronted with other medical, social or psychological issues that the investigator believed could have interfered with study treatment or follow-up. These reasons had to be documented. An example included adherence to a theological or personal doctrine with aversion or opposition to blood transfusion
- Patient had a prior AAA repair (endovascular or surgical)
- Patient had an untreatable allergy or sensitivity to contrast media, Nitinol/nickel, or polyester
- Patient had undergone other major surgical or medical intervention within 45 days of the planned procedure or was planning to undergo other major surgical or medical intervention within 45 days post implantation (e.g., coronary artery bypass grafting, organ transplantation, renal stenting)

2. Follow-up Schedule

All patients were scheduled to return for follow-up examinations at 30 days (+/- 4 weeks), 6 months (+/- 8 weeks), 12 months (+/- 8 weeks), and annually through 5 years (+/- 12 weeks) postoperatively. Additional annual follow-up examinations through 10 years will be conducted for patients who experienced a stent-strut or barb fracture within the first 5 years of study participation. Adverse events and complications were recorded at all visits.

Preoperatively – Each patient was required to have a CT with contrast, a physical examination and ankle-brachial index (ABI), coagulation (PT & APTT), chemistry (BUN & creatinine), and urine human chorionic gonadotropin (hCG) (if applicable).

Treatment and discharge – During the implant procedure, each patient was to have an intraoperative angiogram. Device assessment by the investigator was collected, including: device delivery, deployment, patency, and integrity. At the time of the procedure and prior to hospital discharge, clinical utility data was documented, consisting of: type of anesthesia, duration of procedure, amount of contrast administered, total fluoroscopy time, estimated blood loss, vascular access site, duration of hospitalization, duration of ICU stay. Prior to hospital discharge, each patient was to have a physical examination and ABI.

Post-operative follow-up visits – Assessments during the study included CT with and without contrast and x-rays. At follow-up visits through 12 months, patients were to also have a physical examination and ABI.

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

- Adverse events, including:
    - Serious adverse events
    - Major adverse events
    - Procedure-related adverse events
- Device-related adverse events
- Aneurysm sac rupture
- Stent graft migration, assessed by an Independent Core Lab
- Endoleak, assessed by an Independent Core Lab
- AAA enlargement
- Stent-graft integrity, assessed by an Independent Core Lab
- Loss of stent-graft patency
- Conversion to open surgery
- Secondary interventions
- AAA-related mortality

Pre-operative and post-operative parameters measured for all visits are presented in **Table 7**.

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

Table 7. Schedule of Activities

Assessment	Screening/ Baseline	Treatment	Hospital Discharge	1, 6, & 12 Month Follow-up	Annual Follow-up Visits (Years 2-5 for all patients, and Years 6-10 for patients with Core Lab-confirmed fracture)
Obtain Informed Consent/ Screening Consent	**X**				
Review Medical History and Risk Factors, CT, and Physical Assessment	**X[a]**				
Lab Evaluations	**X**				
Concomitant meds	**X**	**X**			
Physical Exam including Femoral & Pedal Pulses, Ankle-Brachial Index	**X**		**X**	**X[b]**	
CT with and without contrast				**X[c]**	**X[c]**
Cardiac-gated CT (optional)	X			X	X
Angiogram		**X**			
Device Assessment		**X**			
Document clinical utilities		**X**	**X**		
Document ICU time and hospital time			**X**		
AE observation, evaluation, and treatment		**X**	**X**	**X**	**X**
X-ray (KUB, 3-4 view)				**X**	**X**

[a] *Screening CT may be used as the Baseline CT as long as the Screening CT was performed within 4 months of the planned procedure date and includes contrast imaging. If the procedure is delayed and the CT is older than 4 months, or it does not include contrast imaging, an additional CT must be performed for the Baseline evaluation.*

[b] *Incision site assessment only required to be performed at the 1-month follow-up visit*

[c] *Patients with renal insufficiency may be followed with unenhanced CT combined with duplex ultrasound or MRI*

3. Clinical Endpoints

With regard to safety, the primary safety endpoint was the incidence of major adverse events (MAEs) at 30 days post-implant. A major adverse event was defined as any one of the following:

- All-cause mortality
- Myocardial infarction
- Stroke
- Renal failure
- Respiratory failure
- Paraplegia
- Bowel ischemia
- Procedural blood loss of 1,000 cc or greater

The primary safety endpoint was compared to a performance goal of 19%.

With regard to effectiveness, the primary effectiveness endpoint, was successful aneurysm treatment, which was a composite endpoint defined as the following:

- Technical success at the conclusion of the procedure, where the endovascular graft must be patent, with absence of Type I/III endoleak, or treated aneurysm sac rupture
- Absence of aneurysm enlargement (>5 mm) or stent-graft migration (>10 mm) through 12 months (compared to 30-day imaging)
- Absence of fracture, conversion to open surgical repair, treated aneurysm rupture, Type I/III endoleak, or treated stent-graft occlusion through 12 months

The primary effectiveness endpoint was compared to a performance goal of 88%.

With regard to success/failure criteria, the TREO Pivotal Study was considered successful if both the primary safety and effectiveness goals were met.

The following secondary analyses were completed using descriptive statistics:

The secondary safety endpoints included the following:

- The rate of each individual component of the composite MAE, determined at 30 days, 6 months, and 12 months
- The composite MAE rate at 12 months and annually to 5 years
- Procedure-related complications through 30 days, 6 months, 12 months, and annually to 5 years

The secondary effectiveness endpoints included the following:

- Technical success at 30 days confirmed by an imaging modality
- Clinical utility measures (type of anesthesia, procedure duration, time in the intensive care unit and length of hospital stay)
- Aneurysm-related Mortality (ARM) at 12 months and annually through 5 years
- Secondary interventions through 12 months, and annually through 5 years
- Major device-related events through 30 days, 12 months, and annually through 5 years

B. Accountability of PMA Cohort

At the time of database lock, of 150 patients enrolled in the PMA study, 96% (144) of patients were available for analysis at the completion of the study, the 12-month post-operative visit. Of the 144, a total of 131 (91.0%) patients had follow-up imaging deemed evaluable for endovascular graft parameters.

One hundred and fifty patients (150) were implanted with the TREO Abdominal Stent-Graft System and seen through discharge. All of these patients completed the 1-month follow-up visit (minimum of 97% of patients had imaging adequate to evaluate endovascular graft parameters). The follow-up compliance rate of patients with imaging adequate to evaluate endovascular graft parameters at 6 months and 1 year was at least 89.3% and 88.9%, respectively. There were four patients that died within the first year; none of these deaths were aneurysm-related.

Beyond the 1-year visit, there was at least 83% of patients with imaging adequate to assess endovascular graft parameters at 2-years, 71% at 3 years (with 5.8% of patients still in the follow-up window with visit not yet completed), and 40.6% at 4 years (with approximately 31.9% of patients still in the follow-up window with a visit not yet completed). Compliance and imaging follow-up are provided in **Table 8.**

Table 8. Summary of Compliance and Core Lab Imaging Follow-Up

Analysis Window	Patient Follow-Up[c]				Imaging Performed[c]		Imaging Adequate to Assess the Parameter[d]				Events Occurring Within Window[e]				
	Eligible for Visit[a]	No Visit, Still in Window[b]	Missed Visit	Visit Performed	CT Scan	X-Ray	Sac Diameter	Endoleak	Migration	Fracture	Death	Surgical Conversion	LTFU	Early Withdrawal	Not Due for Next Visit
Proc	150	0	0	150/150 (100.0%)	NA	NA	NA	NA	NA	NA	0	0	0	0	0
1 Mo	150	0	0	150/150 (100.0%)	150/150 (100.0%)	147/150 (98.0%)	NA[d]	146/150 (97.3%)	NA[d]	148/150 (98.7%)	1	0	0	0	0
6 Mos	149	0	10/149 (6.7%)	139/149 (93.3%)	138/149 (92.6%)	133/149 (89.3%)	137/149 (91.9%)	134/149 (89.9%)	134/149 (89.9%)	133/149 (89.3%)	2	0	0	3	0
1 Yr	144	0	7/144 (4.9%)	137/144 (95.1%)	137/144 (95.1%)	131/144 (91.0%)	136/144 (94.4%)	133/144 (92.4%)	128/144 (88.9%)	131/144 (91.0%)	7	0	2	3	0
2 Yrs	132	0	13/132 (9.8%)	119/132 (90.2%)	119/132 (90.2%)	113/132 (85.6)	116/132 (87.9%)	113/132 (85.6%)	111/132 (84.1%)	110/132 (83.3%)	6	0	1	5	0
3 Yrs	120	7/120 (5.8%)	15/120 (12.5%)	98/120 (81.7%)	95/120 (79.2%)	88/120 (73.3%)	94/120 (78.3)	94/120 (78.3%)	91/120 (75.8%)	86/120 (71.7%)	2	0	2	3	44
4 Yrs	69	22/69 (31.9%)	8/69 (11.6%)	39/69 (56.5%)	32/69 (46.4%)	30/69 (43.5)	30/69 (43.5)	31/69 (44.9%)	28/69 (40.6%)	30/69 (43.5%)	0	0	2	5	49
5 Yrs	13	10/13 (76.9%)	2/13 (15.4%)	1/13 (7.7%)	1/13 (7.7%)	1/13 (7.7%)	1/13 (7.7%)	1/13 (7.7%)	1/13 (7.7%)	1/13 (7.7%)	0	0	0	1	0

NA – Not Applicable

[a] Eligible for Visit reflects those patients eligible for follow-up calculated as: (previous eligible for follow-up) – (previous death + conversion + lost to follow-up + early withdrawal + not due for follow-up)

[b] Patients who did not have a visit within the window but who had not yet reached the end of the analysis window. This value is used for the denominator for calculating the percentage of visits performed.

[c] Based on site-reported data

[d] Based on Core Laboratory analysis. Sac Diameter and Migration assessments use 1 month as baseline, and are therefore not reported at 1 month. Eligible patients require valid value at 1 month and at the specified time point.

[e] These columns reflect patients who had visits within the specified window but were not eligible at the start of the next window due to death, surgical conversion, lost to follow-up or early withdrawal.

C. Study Population Demographics and Baseline Parameters

Demographics

The demographics of the study population are typical for an EVAR pivotal study performed in the US. In the study, 88% (132/150) of patients were male. The mean age was 71.7 years and approximately one-half of the patients were between 65 and 74 years of age. Almost all patients were Caucasian, 98.0% (147/150). Patient demographics for the study are provided in **Table 9**.

Table 9. Summary of Patient Demographics

Characteristic	Statistics	Pivotal
Sex		
Female	% (n/N)	12.0% (18/150)
Male	% (n/N)	88.0% (132/150)
Age (years)	Mean ± SD (N) Median (IQR) Min - Max	71.7 ± 7.4 (150) 72.0 (67.0, 78.0) 52 - 85
Age Groups		
18-64 years	% (n/N)	16.7% (25/150)
65-74 years	% (n/N)	48.0% (72/150)
75-80 years	% (n/N)	24.7% (37/150)
81-85 years	% (n/N)	10.7% (16/150)
Ethnic Group		
Hispanic or Latino	% (n/N)	1.3% (2/150)
Not Hispanic or Latino	% (n/N)	96.7% (145/150)
Not Reported	% (n/N)	1.3% (2/150)
Unknown	% (n/N)	0.7% (1/150)
Race		
American Indian/Alaskan Native	% (n/N)	0.7% (1/150)
Black or African American	% (n/N)	1.3% (2/150)
White	% (n/N)	98.0% (147/150)

Baseline Medical History

The baseline clinical history for the study patients is summarized in **Table 10.** Most of the patients in the study had a history of hypertension (90.0%, 135/150) or received treatment for hypertension (73.3%, 110/150). A history of hyperlipidemia was reported in 73.3% (110/150) and smoking in 85.3% (128/150).

Table 10. Summary of Patient Medical History

Comorbidity	Pivotal
Peripheral Vascular Disease	25.3% (38/150)
Documented Coronary Artery Disease	56.0% (84/150)
Myocardial Infarction	18.0% (27/150)
Stable Angina	0.7% (1/150)
Unstable Angina	6.0% (9/150)
Arrhythmias	24.0% (36/150)
Congestive Heart Failure	8.7% (13/150)
Other	32.2% (48/149)
Diabetes Mellitus	28.0% (42/150)
Hypertension (HTN) and/or Treatment of HTN	90.0% (135/150)
Hypercholesterolemia	44.7% (67/150)
Hyperlipidemia	73.3% (110/150)
Smoking	85.3% (128/150)
Current	31.3% (40/128)
Former	68.8% (88/128)
Renal Insufficiency	13.3% (20/150)
Currently on Antiplatelet/Anticoagulant Medications	78.7% (118/150)
Limb Ischemia	7.3% (11/150)
Limb Ischemia: Left Claudication	6.0% (9/150)
Limb Ischemia: Left Ischemic Rest Pain	0.7% (1/150)
Limb Ischemia: Left Asymptomatic	2.0% (3/150)
Limb Ischemia: Right Claudication	5.3% (8/150)
Limb Ischemia: Right Ischemic Rest Pain	0.7% (1/150)
Limb Ischemia: Right Asymptomatic	2.7% (4/150)
Vascular Intervention	18.0% (27/150)
Gastrointestinal	20.0% (30/150)
Cholecystitis	4.0% (6/150)
Ischemic Colitis	0% (0/150)
Complications: Small Bowel Ischemia	0.7% (1/150)
GI Bleed	4.7% (7/150)
Impotence	16.0% (24/150)

Comorbidity	Pivotal
All values expressed as % (n/N)	

Baseline Vessel Measurements

A comparison of the Core Laboratory and site reported baseline aneurysm and anatomical measurements are provided in **Table 11.** Patients with aortic or aortoiliac aneurysms were enrolled in the study. All patients met the inclusion criteria for study entry, with the exception of one who had pre-existing chronic obstructive lung disease for which he denied daily oxygen use prior to enrollment, as he used oxygen only as needed during the day. However, following enrollment, the patient clarified that he used oxygen every night, which constituted routine oxygen use, and was an exclusion criterion. Of the 150 patients enrolled in the study, 19 (12.7%) had iliac artery involvement.

Table 11. Comparison of Core Laboratory and Site Reported Anatomic Characteristics

Characteristic	Statistics	Core Laboratory	Site Reported
Angle between Suprarenal Aorta and Proximal AAA Neck (degrees) (Suprarenal Neck Angle)	Mean ± SD (N) Median (IQR) Min - Max	18.6 ± 11.1 (149) 16.4 (10.1, 25.8) 0.0 - 51.9	13.0 ± 11.1 (149) 10.0 (3.0, 20.0) 0.0 - 40.0
Angle between Proximal AAA Neck and Main Axis of AAA (degrees) (Infrarenal Neck Angle)	Mean ± SD (N) Median (IQR) Min - Max	35.8 ± 13.2 (149) 35.4 (27.2, 42.0) 5.2 - 72.2	25.0 ± 16.5 (149) 22.0 (12.0, 35.0) 0.0 - 70.0
Diameter of Proximal Neck (mm)	Mean ± SD (N) Median (IQR) Min - Max	23.0 ± 3.1 (150) 22.3 (21.0, 24.7) 15.0 - 33.5	23.7 ± 3.0 (150) 24.0 (21.5, 25.0) 17.0 - 32.0
Length of Infrarenal Proximal Neck (mm) (Proximal Landing Zone)	Mean ± SD (N) Median (IQR) Min - Max	43.1 ± 13.0 (150) 43.1 (33.9, 50.7) 14.4 - 80.4	28.4 ± 11.2 (150) 27.8 (20.0, 34.0) 10.0 - 60.0
Length from Lowest Renal Artery to Aortic Bifurcation (mm)	Mean ± SD (N) Median (IQR) Min - Max	119.5 ± 14.2 (150) 118.5 (110.6, 127.5) 85.1 - 160.8	116.8 ± 16.0 (150) 114.0 (107.5, 124.0) 90.0 - 200.0
Length from Aortic Bifurcation to Right Internal Iliac Artery (mm)	Mean ± SD (N) Median (IQR) Min - Max	59.4 ± 15.3 (150) 59.5 (47.9, 71.8) 25.9 - 95.5	64.1 ± 30.4 (150) 58.2 (46.0, 73.0) 25.0 - 185.0
Length from Aortic Bifurcation to Left Internal Iliac Artery (mm)	Mean ± SD (N) Median (IQR) Min - Max	58.5 ± 15.7 (149) 57.7 (48.8, 66.7) 26.9 - 107.9	64.5 ± 29.4 (149) 58.0 (47.0, 71.0) 30.0 - 192.0
Length of Right Iliac/Femoral Landing Zone (mm)	Mean ± SD (N) Median (IQR) Min - Max	48.9 ± 19.8 (136) 48.6 (33.5, 63.8) -14.9 - 94.0	37.6 ± 21.6 (136) 30.0 (20.0, 50.5) 4.0 - 120.0
Length of Left Iliac/Femoral Landing Zone (mm)	Mean ± SD (N) Median (IQR) Min - Max	50.6 ± 19.1 (140) 51.3 (35.8, 61.8) 13.7 - 107.9	38.6 ± 21.3 (140) 37.5 (20.0, 50.0) 6.0 - 120.0
Total Treatment Length (Core Lab = One Measure, Site = Left) (mm)	Mean ± SD (N) Median (IQR) Min - Max	187.9 ± 20.2 (150) 186.9 (172.9, 202.6) 139.3 - 265.4	181.0 ± 32.8 (150) 174.0 (158.0, 194.0) 137.0 - 336.0

Table 11. Comparison of Core Laboratory and Site Reported Anatomic Characteristics

Characteristic	Statistics	Core Laboratory	Site Reported
Total Treatment Length (Core Lab = One Measure, Site = Right) (mm)	Mean ± SD (N) Median (IQR) Min - Max	187.9 ± 20.2 (150) 186.9 (172.9, 202.6) 139.3 - 265.4	181.0 ± 33.8 (150) 174.0 (160.0, 198.0) 130.0 - 329.0
Maximum Aneurysm Diameter (mm)	Mean ± SD (N) Median (IQR) Min - Max	54.0 ± 7.7 (150) 52.8 (50.0, 56.4) 39.2 - 113.3	54.4 ± 6.6 (150) 53.2 (51.0, 57.0) 42.4 - 108.0
Diameter of Distal Aorta (mm) (Aortic Diameter at Bifurcation)	Mean ± SD (N) Median (IQR) Min - Max	30.4 ± 9.5 (150) 28.2 (23.3, 35.7) 16.7 - 72.1	26.5 ± 6.3 (150) 25.0 (22.0, 30.0) 15.0 - 47.0
Diameter of Right Iliac Landing Zone Neck (mm)	Mean ± SD (N) Median (IQR) Min - Max	16.9 ± 3.0 (145) 16.6 (14.7, 18.7) 9.6 - 27.3	14.1 ± 2.8 (145) 14.0 (12.0, 16.0) 9.0 - 23.0
Diameter of Left Iliac Landing Zone Neck (mm)	Mean ± SD (N) Median (IQR) Min - Max	17.4 ± 3.8 (145) 16.4 (15.0, 19.1) 11.1 - 36.1	13.7 ± 2.6 (145) 14.0 (12.0, 15.0) 8.0 - 20.0

The distribution of baseline aneurysm diameters as measured by the Imaging Core Laboratory is presented in **Table 12**. The majority of patients (100/150, 66.7%) had aneurysms with maximum sac diameter ranging from 50-59 mm.

Table 12. Distribution of Baseline Aneurysm Diameters – Core Lab Reported

Maximum Aneurysm Diameter (mm)	Pivotal Study N = 150
< 45 mm	3/150 (2.0%)
45-49 mm	27/150 (18.0%)
50-59 mm	100/150 (66.7%)
60-69 mm	15/150 (10.0%)
70-79 mm	4/150 (2.7%)
80-89 mm	0
≥ 90 mm	1/150 (0.7%)

TREO Devices Implanted

A total of 565 TREO Stent-Grafts were implanted in the Pivotal Study. The number and types of TREO Stent-Grafts implanted in the initial procedure are shown in **Tables 13 and 14**. No competitor devices were implanted during any of the initial procedures. All patients received at least 3 TREO Stent-Grafts; namely, a single Main Bifurcated Stent-Graft and 2 Leg Extension Stent-Grafts. Ten percent of patients received additional stent-grafts (13 patients received 1 additional stent-graft, 1 patient received 2 additional stent-grafts and 1 patient received 3 additional stent-grafts). Overall, 98.7% of the patients were treated with 3 or 4 total TREO Stent-Grafts.

The diameters of the devices implanted in the Pivotal Study are show in **Table 15**.

Table 13. TREO Stent-Grafts Implanted

TREO Components	Pivotal Study N = 150*
Main Bifurcated Stent-Graft	150/150 (100.0%)
Proximal Cuff Stent-Graft	6/150 (4.0%)
Ipsilateral Leg Extension Stent-Graft	150/150 (100.0%)
Ipsilateral Leg/Straight Extension Stent-Graft	3/150 (2.0%)
Contralateral Leg Extension Stent-Graft	150/150 (100.0%)
Contralateral Leg/Straight Extension Stent-Graft	7**/150 (4.7%)
Denominator includes all patients who received the test device.* * Seven patients received 9 contralateral Leg Extension Stent-Grafts / Straight Extension Stent-Grafts*	

Table 14. Number of Devices Implanted During the Index Procedure

Number of Devices Implanted	Pivotal Cohort N = 150*
1	NA
2	NA
3	135/150 (90.0%)
4	13/150 (8.7%)
5	1/150 (0.7%)
6	1/150 (0.7%)
**Denominator includes all patients who received the TREO device.*	

Table 15. Diameter of TREO Devices Implanted During the Index Procedure

TREO Stent-Graft Type	Outer Diameter (mm)	Pivotal Study N = 150*
Main Bifurcated Stent-Graft		150/150 (100.0%)
	20	1/150 (0.7%)
	22	5/150 (3.3%)
	24	12/150 (8.0%)
	26	34/150 (22.7%)
	28	48/150 (32.0%)
	30	24/150 (16.0%)
	33	19/150 (12.7%)
	36	7/150 (4.7%)
Proximal Cuff Stent-Graft		6/150 (4.0%)
	20	0/150 (0.0%)
	22	0/150 (0.0%)
	24	0/150 (0.0%)
	26	2/150 (1.3%)
	28	2/150 (1.3%)

Table 15. Diameter of TREO Devices Implanted During the Index Procedure

TREO Stent-Graft Type	Outer Diameter (mm)	Pivotal Study N = 150*
	30	0/150 (0.0%)
	33	2/150 (1.3%)
	36	0/150 (0.0%)
Ipsilateral Leg Extension Stent-Graft		150/150 (100%)
	9	2/150 (1.3%)
	11	4/150 (2.7%)
	13	23/150 (15.3%)
	15	45/150 (30.0%)
	17	36/150 (24.0%)
	20	26/150 (17.3%)
	24	14/150 (9.3%)
Contralateral Leg Extension Stent-Graft		150/150 (100%)
	9	1/150 (0.7%)
	11	12/150 (8.0%)
	13	25/150 (16.7%)
	15	39/150 (26.0%)
	17	34/150 (22.7%)
	20	17/150 (11.3%)
	24	12/150 (8.0%)
Ipsilateral Leg/Straight Extension Stent-Graft		3/150 (2.0%)
	9	0/150 (0.0%)
	11	1/150 (0.7%)
	13	1/150 (0/7%)
	15	0/150 (0.0%)
	17	0/150 (0.0%)
	20	1/150 (0.7%)
	24	0/150 (0.0%)
Contralateral Leg/Straight Extension Stent-Graft		7**/150 (4.7%)
	9	1/150 (0.7%)
	11	0/150 (0.0%)
	13	0/150 (0.0%)
	15	2/150 (1.3%)
	17	3/150 (2.0%)
	20	3/150 (2.0%)
	24	0/150 (0.0%)

** Denominator included all patients who received the TREO device*
*** Seven patients received 9 Leg Extensions / Straight Extensions*

Procedural Data

Detailed information and observations about the index procedure were documented by physicians on case report forms. **Table 16** summarizes information from the index procedure, including clinical utility endpoints. The majority of patients underwent general anesthesia, (88.7% (133/150)). The mean procedure time was 105.7 minutes. The patient outcomes were favorable, with a mean estimated blood loss of 168 mL. The mean ICU stay was 3.3 hours and the mean length of hospital stay was 2.5 days.

Table 16. Summary of Index Procedure

Characteristic	Statistics	Pivotal
Type of Anesthesia		
General	% (n/N)	88.7% (133/150)
Local	% (n/N)	6.7% (10/150)
Regional/Epidural	% (n/N)	2.0% (3/150)
Other	% (n/N)	2.7% (4/150)
Duration of Procedure (min)	Mean ± SD (N) Median (IQR) Min - Max	105.7 ± 43.6 (150) 93.5 (72.0, 127.0) 35.0 - 284.0
Amount Contrast Administered (cc)	Mean ± SD (N) Median (IQR) Min - Max	100.4 ± 53.7 (149) 88.0 (62.0, 120.0) 30.0 - 330.0
Total Fluoroscopy Time (min)	Mean ± SD (N) Median (IQR) Min - Max	19.8 ± 9.4 (150) 18.0 (14.4, 22.5) 7.3 - 69.3
Estimated Blood Loss (cc)	Mean ± SD (N) Median (IQR) Min - Max	167.5 ± 172.2 (150) 100.0 (50.0, 200.0) 0.0 - 1,000.0
Anticoagulation, Antiplatelet, Antibiotic Given	% (n/N)	98.0% (147/150)
Main Bifurcate Access		
Left Femoral	% (n/N)	13.3% (20/150)
Right Femoral	% (n/N)	86.0% (129/150)
Right Iliac	% (n/N)	0.7% (1/150)
Contralateral Access		
Left Femoral	% (n/N)	86.0% (129/150)
Right Femoral	% (n/N)	13.3% (20/150)
Right Iliac	% (n/N)	0.7% (1/150)
Internal Iliac Artery Covered		
No	% (n/N)	91.3% (137/150)
Yes	% (n/N)	8.7% (13/150)
Left	% (n/N)	46.2% (6/13)
Right	% (n/N)	53.8% (7/13)
Duration of Hospitalization (days)	Mean ± SD (N) Median (IQR) Min - Max	2.5 ± 1.2 (150) 2.0 (2.0, 2.0) 1.0 - 10.0
Duration of ICU Stay (hours)	Mean ± SD (N) Median (IQR) Min - Max	3.3± 13.7 (150) 0.0 (0.0, 0.0) 0.0 – 124.0

D. Safety and Effectiveness Results

1. Safety Results

1.1 Primary Safety Endpoint

The analysis of safety was based on the TREO Pivotal Study cohort of 150 patients (i.e., all patients who had the Main Bifurcated Stent-Graft introduced into the body) available for the 30-day (1-month) evaluation. The key safety outcomes for this study are presented below in **Table 17** and **Table 18.** Adverse effects are reported in **Tables 19 to 22.**

The Primary Safety Endpoint was the major adverse event (MAE) rate at 30 days post-procedure compared to a performance goal of 19%. Patients who experienced at least 1 MAE through 30 days were included in the primary safety analysis even if the patient had not completed a 1-month follow-up visit. The composite MAE rate through 30 days was 0.7% (1/150), meeting the pre-specified performance goal. There was one patient with 2 MAEs, specifically myocardial infarction and procedural blood loss of 1,000 cc; no other MAE components (i.e., all-cause mortality, stroke, renal failure requiring renal replacement therapy, respiratory failure, paraplegia, bowel ischemia) were reported through 30 days.

Table 17. 30-Day Composite Major Adverse Events

Characteristics	Statistics	Pivotal Study
MAE Rate at 30 Days	% (n/N)	0.7% (1/150)
	95% CI	0.0%, 3.7%
	P value	<0.0001
Time to MAE Analysis		
Number with Events	n	1
Censored	n	0
At Risk	n	149*
Kaplan-Meier Estimate of MAE within 30 days	% (95% CI)	0.7% (0.1%, 4.6%)

MAE – Major Adverse Events

All MAEs were adjudicated by the Clinical Events Committee (CEC)

**Number of patients at risk at 30 days (150 – 1 patient with event within 30 days)*

Table 18 summarizes the individual components of the MAE composite endpoint through 30 days.

Table 18. Summary of Major Adverse Event Components through 30 Days

MAE Components	Statistics	Pivotal (N=150)
Patients with any MAE	% (n/N)	0.7% (1/150)
All-cause mortality	% (n/N)	0
Myocardial infarction	% (n/N)	0.7% (1/150)*
Stroke	% (n/N)	0
Renal failure requiring renal replacement therapy	% (n/N)	0
Respiratory failure	% (n/N)	0
Paraplegia	% (n/N)	0
Bowel Ischemia	% (n/N)	0
Procedural blood loss of 1,000 cc or greater	% (n/N)	0.7% (1/150)*

MAE – Major Adverse Events

All MAEs were adjudicated by the Clinical Events Committee (CEC).

** Patient experienced procedural blood loss of 1,000cc during the implant procedure, which required a blood transfusion. The treating investigator reported no complications during the procedure. The CEC/DSMB adjudicated the procedural blood loss as not related to device but definitely related to the implant procedure. The patient also experienced an MI 12 days post procedure and recovered.*

1.2 Secondary Safety Endpoints

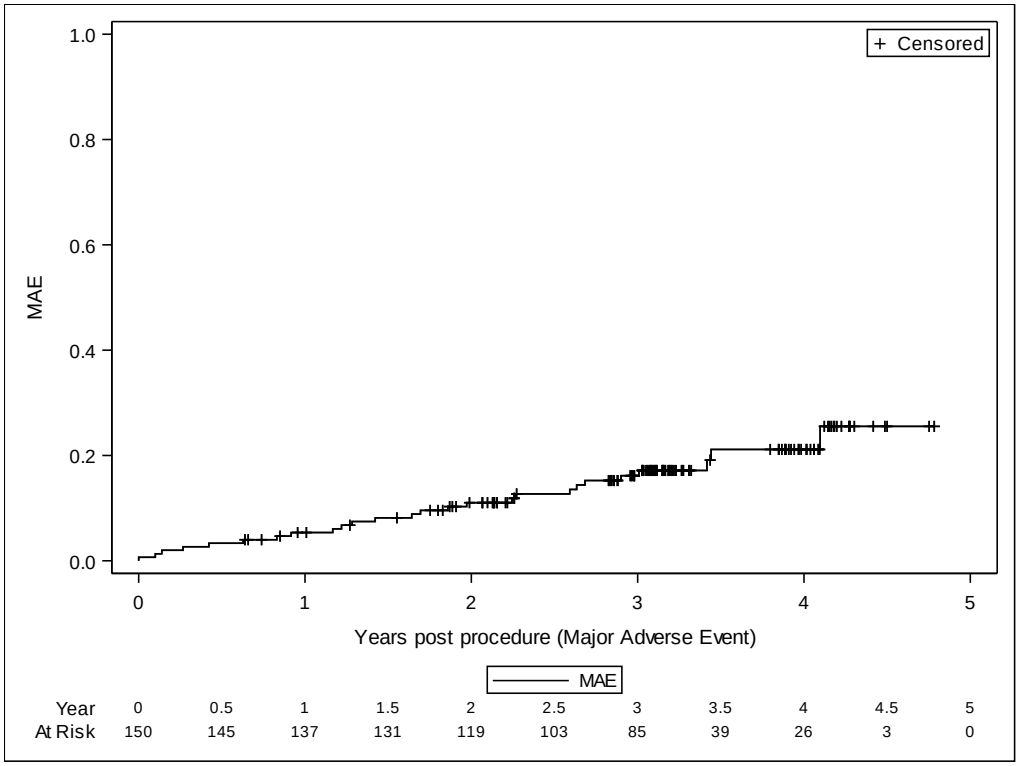
1.2.1 Major Adverse Events

The individual components of the MAE composite endpoint (**Table 19**) and a Kaplan-Meier estimate of the MAE rates from the Pivotal Study are presented in this section. MAE rate throughout follow-up is depicted in **Figure 5** as a Kaplan-Meier plot. Kaplan-Meier estimates of the MAE rates were 0.7% at 30 days, 5.4% at 12 months, 11.0% at 2 years, 16.2% at 3 years, and 21.2% at 4 years. The most common event was death unrelated to the device or to the procedure, occurring in 18 patients through 5 years and accounting for 18 of the 26 reported MAEs (69.2%).

Table 19. Summary of Major Adverse Events By Timepoint

Characteristic	Procedure	30 Days	6 Months	1 Year	2 Years	3 Years	4 Years	5 Years	Total[a]
Number of Patients Eligible[b]	150	150	150	148	141	123	91	28	150
Number of Patients with any MAE	1 (0.7%)	1 (0.7%)	4 (2.7%)	4 (2.7%)	9 (6.4%)	7 (5.7%)	4 (4.4%)	1 (12.5%)	27
Death (all-cause)	0	0	2 (1.3%)	2 (1.4%)	8 (5.7%)	4 (3.3%)	2 (2.2%)	0	18
Stroke	0	0	1 (0.7%)	1 (0.7%)	4 (2.8%)	2 (1.6%)	1 (1.1%)	1 (12.5%)	10
Myocardial Infarction	0	1 (0.7%)	0	2 (1.4%)	1 (0.7%)	1 (0.8%)	1 (1.1%)	0	5
Bowel Ischemia	0	0	1 (0.7%)	0	0	0	0	0	1
Respiratory Failure	0	0	0	1 (0.7%)	0	1 (0.8%)	0	0	2
Procedural blood loss of 1000cc or more	1 (0.7%)	0	0	0	0	0	0	0	1
Paraplegia	0	0	0	0	0	0	0	0	0
Renal Failure	0	0	0	0	0	0	0	0	0

[a] *Cumulative number of patients with the event type. Note that some patients had more than one event at more than one timepoint.*
[b] *Number of Patients eligible for each timepoint reflects the number of patients that were active in the study for a given timepoint, regardless if a visit was completed during that interval.*



Time	Failure Rate	Lower 95% CI	Upper 95% CI	MAE	At Risk
Procedure	0.67%	0.09%	4.64%	1	149
30 Days	0.67%	0.09%	4.64%	1	149
6 Months	3.33%	1.40%	7.82%	5	145
12 Months	5.37%	2.72%	10.45%	8	137
1.5 Years	8.16%	4.72%	13.93%	12	131
2 Years	11.04%	6.91%	17.40%	16	119
2.5 Years	12.70%	8.18%	19.44%	18	119
3 Years	16.17%	10.91%	23.60%	22	85
3.5 Years	21.15%	14.22%	30.78%	25	26
4 Years	21.15%	14.22%	30.78%	25	26
5 Years	.	.	.	26	0

Figure 5. Kaplan-Meier Plot of Major Adverse Event Rate: Pivotal Study

1.2.2 Device-Related Adverse Events

Device-related AEs were adjudicated by the CEC and are summarized in **Table 20**. There were 16.0% (24/150) of patients with at least one device-related AE reported. The majority, 5.3% (8/150), of device-related AEs reported were due to stent-graft endoleaks.

Table 20. Summary of Device-Related Adverse Events

MedDRA SOC/PT	Pivotal (N=150) n (%)
Patients with at least one Device-Related AE	24 (16.0%)
General Disorders and Administration Site Conditions	16 (10.7%)
Device Breakage	6 (4.0%)
Device Occlusion	1 (0.7%)
Pyrexia	1 (0.7%)
Stent-Graft Endoleak	8 (5.3%)
Vascular Complication Associated with Device	1 (0.7%)
Injury, Poisoning and Procedural Complications	3 (2.0%)
Re-occlusion	2 (1.3%)
Vascular Graft Occlusion	1 (0.7%)
Renal and Urinary Disorders	3 (2.0%)
Renal Artery Aneurysm	1 (0.7%)
Renal Artery Occlusion	1 (0.7%)
Renal Artery Stenosis	1 (0.7%)
Vascular Disorders	5 (3.3%)
Aneurysm	1 (0.7%)
Arterial Stenosis	1 (0.7%)
Arterial Thrombosis	1 (0.7%)
Embolism	2 (1.3%)
Intermittent Claudication	1 (0.7%)
Peripheral Artery Stenosis	0 (0.0%)
Peripheral Ischemia	1 (0.7%)

Table 20. Summary of Device-Related Adverse Events

MedDRA SOC/PT	Pivotal (N=150) n (%)
All device-related AEs were adjudicated by the CEC. The core laboratory assessed events evaluated through imaging such as, endoleaks, fractures, and occlusions.	
Percentages are based on the number of patients in the Safe Evaluable Population (Pivotal and Continued Access).	
Medical Dictionary for Regulatory Activities (MedDRA) version 18.0 was used for coding adverse events.	
A patient who experienced multiple events within a SOC (System Organ Classes – groupings by etiology, manifestation site or purpose) or PT (Preferred Terms – distinct descriptor for a symptom, sign, disease diagnosis, therapeutic indication, investigation, surgical or medical procedure, and medical social or family history characteristic) is counted once for that class and once for the PT.	
A device-related AE is one whose relationship to device is possibly or definitely related. Missing relationship to device is considered "unknown."	

1.2.3 Procedure-Related Adverse Events

Procedure-related AEs were adjudicated by the CEC and are summarized in **Table 21.** There were 34.7% (52/150) of patients with at least one procedure-related AE reported. The majority of procedure-related AEs reported were vascular disorders, 9.3% (14/150) and general disorders and administration site conditions, 8.7% (13/150).

Table 21. Summary of Procedure-Related Adverse Events

MedDRA SOC/PT	Pivotal Patients (N=150) n (%)
Patients with at least one Procedure-Related AE	52 (34.7%)
Blood and Lymphatic System Disorders	1 (0.7%)
Leukocytosis	1 (0.7%)
Cardiac Disorders	2 (1.3%)
Atrial Fibrillation	1 (0.7%)
Myocardial Infarction	1 (0.7%)
Gastrointestinal Disorders	6 (4.0%)
Abdominal Pain	1 (0.7%)
Colitis Ischemic	1 (0.7%)
Constipation	2 (1.3%)
Dyspepsia	1 (0.7%)
Ileus	1 (0.7%)
General Disorders and Administration Site Conditions	13 (8.7%)
Device Occlusion	1 (0.7%)
Medical Device Site Discharge	1 (0.7%)

Table 21. Summary of Procedure-Related Adverse Events

MedDRA SOC/PT	Pivotal Patients (N=150) n (%)
Pyrexia	7 (4.7%)
Stent-Graft Endoleak	3 (2.0%)
Vascular Complication Associated with Device	2 (1.3%)
Infections and Infestations	5 (3.3%)
Groin Infection	1 (0.7%)
Pneumonia	1 (0.7%)
Post Procedural Pneumonia	1 (0.7%)
Urinary Tract Infection	2 (1.3%)
Injury, Poisoning and Procedural Complications	9 (6.0%)
Arterial Injury	1 (0.7%)
Incision Site Pain	1 (0.7%)
Procedural Nausea	1 (0.7%)
Procedural Pain	1 (0.7%)
Reocclusion	2 (1.3%)
Seroma	1 (0.7%)
Vascular Graft Occlusion	1 (0.7%)
Wound	1 (0.7%)
Metabolism and nutrition disorders	1 (0.7%)
Hypokalemia	1 (0.7%)
Musculoskeletal and connective tissue disorders	1 (0.7%)
Pain in extremity	1 (0.7%)
Nervous system disorders	2 (1.3%)
Spinal cord ischemia	2 (1.3%)
Renal and urinary disorders	10 (6.7%)
Acute kidney injury	1 (0.7%)
Hematuria	1 (0.7%)
Micturition urgency	1 (0.7%)
Renal artery occlusion	2 (1.3%)
Renal artery stenosis	1 (0.7%)
Renal infarct	2 (1.3%)
Urinary retention	3 (2.0%)

Table 21. Summary of Procedure-Related Adverse Events

MedDRA SOC/PT	Pivotal Patients (N=150) n (%)
Reproductive system and breast disorders	2 (1.3%)
Genital discomfort	1 (0.7%)
Penile hemorrhage	1 (0.7%)
Respiratory, thoracic and mediastinal disorders	1 (0.7%)
Laryngospasm	1 (0.7%)
Surgical and medical procedures	2 (1.3%)
Wound drainage	2 (1.3%)
Vascular disorders	14 (9.3%)
Aneurysm	2 (1.3%)
Arterial Stenosis	1 (0.7%)
Arteriovenous Fistula	1 (0.7%)
Hematoma	2 (1.3%)
Hemorrhage	1 (0.7%)
Iliac Artery Rupture	1 (0.7%)
Intermittent claudication	1 (0.7%)
Peripheral artery thrombosis	1 (0.7%)
Peripheral ischemia	4 (2.7%)

All procedure-related AEs were adjudicated by the CEC. The core laboratory assessed events evaluated through imaging such as, endoleaks, fractures, and occlusions.

Percentages are based on the number of patients in the Safe Evaluable Population (Pivotal and Continued Access).

MedDRA version 18.0 was used for coding adverse events.

A patient who experienced multiple events within a SOC or PT is counted once for that class and once for the PT.

1.2.4 All-Cause and Aneurysm-Related Mortality

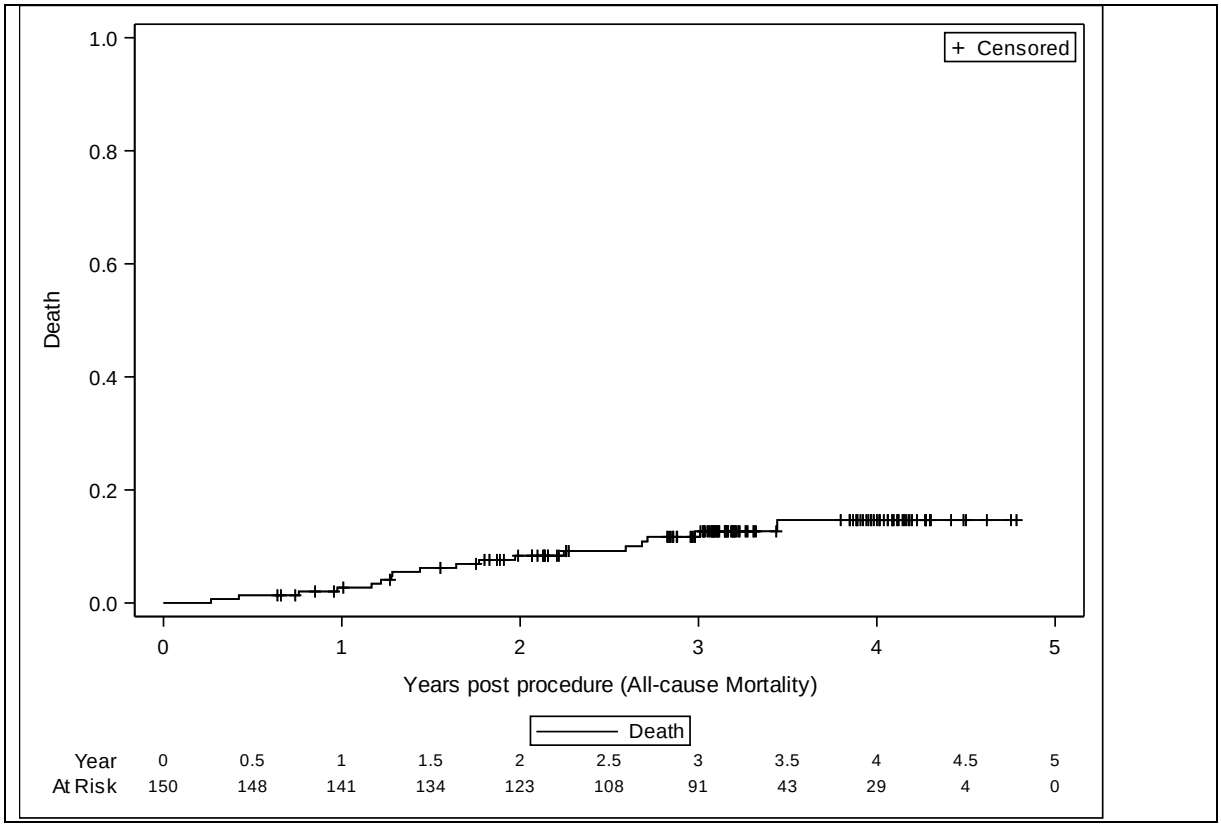
A summary of all-cause mortality and aneurysm-related mortality through follow-up is presented for the Pivotal Study. A Kaplan-Meier estimate of all-cause mortality is presented in **Figure 6.** Aneurysm-related mortality was adjudicated by the CEC. The assessments of all-cause mortality for the study are provided in **Table 22**. There have been 18 deaths in the Pivotal Study, and none were aneurysm-related.

Table 22. All-Cause and Aneurysm-Related Mortality

Deaths	Procedure	30 Days	6 Months	12 Months	2 Years	3 Years	4 Years
All-Cause Deaths							
At Risk	150	150	148	141	123	91	28
Interval	0	0	2	2	8	4	2
Cumulative	0	0	2	4	12	16	18
Aneurysm-Related Deaths*							
Interval	0	0	0	0	0	0	0
Cumulative	0	0	0	0	0	0	0

CEC – Clinical Events Committee

** Aneurysm-related deaths were adjudicated by the CEC.*



Time	Failure Rate	Lower 95% CI	Upper 95% CI	Deaths	At Risk
Procedure	0.00%	.	.	0	150
30 Days	0.00%	.	.	0	150
6 Months	1.33%	0.34%	5.23%	2	148
1 Years	2.70%	1.02%	7.04%	4	141
1.5 Years	6.19%	3.27%	11.57%	9	134
2 Years	8.35%	4.83%	14.24%	12	123
2.5 Years	9.17%	5.42%	15.28%	13	108
3 Years	11.69%	7.31%	18.43%	16	91
3.5 Years	14.65%	9.16%	22.97%	18	43
4 Years	14.65%	9.16%	22.97%	18	28
4.5 Years	14.65%	9.16%	22.97%	18	3
5 Years	.	.	.	18	0

Figure 6. Kaplan-Meier Freedom from All-Cause Mortality: Pivotal Study

2. Effectiveness Results

2.1 Primary Effectiveness

The analysis of effectiveness was based on the 131 patients evaluable for all components of the composite endpoint at the 12-month timepoint. Key effectiveness outcomes are presented in **Table 23** and **Table 24**.

The primary effectiveness endpoint of successful aneurysm treatment was achieved in 93.13% of the TREO Pivotal Study cohort (122/131; 95% CI 87.36% to 96.81%, **Table 23**) through 12 months. The rate of the primary effectiveness endpoint was less than the effectiveness performance goal of 88% (P=0.0400). Of note, the performance goal for the primary effectiveness endpoint for this Pivotal Study was more conservative as compared to other endovascular graft pivotal studies evaluating similar intended patient populations. For example, previous infrarenal endovascular graft studies may have used a performance goal of 80% or not include device fracture as part of the composite endpoint.

Table 23. Successful Aneurysm Treatment at 12 Months

Characteristic	Statistics	Pivotal
Successful Aneurysm Treatment at 12 Months	% (n/N)	93.13% (122/131)
	95% CI	87.36%, 96.81%
	P Value*	0.0400
**P value corresponds to the hypothesis test (at a one-sided level of 0.025) that the observed value is greater than the performance goal of 88%.*		

Table 24 summarizes the components of the primary effectiveness endpoint for the Pivotal Study. Overall, nine patients did not meet the definition of treatment success. The technical success (intra-procedure) rate was 100%. Stent-grafts were patent at the end of procedure in all patients. One patient had a Type Ia endoleak noted at the end of the index procedure, but this was not confirmed by the Imaging Core Laboratory and also present on the 30-day CT scan and, therefore, did not trigger the primary effectiveness endpoint. No patient had aneurysm enlargement exceeding 5 mm, and there were no stent-graft migrations (>10 mm) through 12 months. Type I/III endoleaks were reported by the Core Laboratory in three patients with evaluable CT imaging through 12 months. There were three patients with endograft occlusions requiring reintervention through 12 months (2.1% of 144 patients with evaluable imaging). Stent strut or barb fractures were detected in 4 of 135 (3.0%) patients with evaluable 12-month x-ray imaging. One of the nine patients experienced two endpoint events: a Type Ia endoleak at 44 days post index procedure that was treated with endostaples and a non-TREO aortic cuff, and a stent fracture which was detected at the 6-month follow-up visit.

Table 24. Individual Components of the Composite Primary Effectiveness Endpoint

Components of Primary Endpoint	Pivotal
Composite of Technical Success at Procedure	100.0% (150/150)
No Type I/III Endoleak at Conclusion of Procedure	100.0% (150/150)
Patent Endograft at Procedure	100.0% (150/150)
No Aneurysm Rupture	100.0% (150/150)
Absence of Sac Increase >5 mm through 12 Months*	100.0% (138/138)
Absence of Migration >10 mm through 12 Months*	100.0% (133/133)
Patency without Reintervention through 12 Months	97.9% (141/144) [a, b, c]
Absence of Fracture of Stent or Barb through 12 Months*	97.0% (131/135) [d, e, f, g]
No Type I/III Endoleaks through 12 Months*	97.8% (134/137) [e, h, i]

Table 24. Individual Components of the Composite Primary Effectiveness Endpoint

Components of Primary Endpoint	Pivotal
** Core Laboratory assessed components of the primary effectiveness endpoint in patients with adequate imaging. Adequate imaging was determined by the Core Laboratory. In general, images with contrast were regarded as adequate for interpretation of endograft patency.* *[a] Patient experienced right Leg Extension occlusion, which was treated 12 days post-implant with right common femoral endarterectomy with patch, right common iliac stent with angioplasty, and right common iliac embolectomy. This treatment did not resolve the occlusion, and 79 days post-index procedure patient was successfully treated with left to right femoral to femoral bypass, right proximal superficial femoral artery stent x 2, and right distal superficial femoral artery stent x 2.* *[b] Patient experienced right Leg Extension occlusion, which was initially treated 30 days post-implant with lytic therapy, PTA of thrombosis, and angioplasty of right iliac. Patient was then treated the following day (31 days post-implant) with endovascular revascularization and open right iliac with non-TREO stent-grafts and angioplasty, which resolved the occlusion.* *[c] Patient experienced left proximal iliac artery stent occlusion, which was successfully treated 9 days post-implant with angioplasty and embolectomy.* *[d] Patient experienced a wireform fracture in the proximal aspect of the uncovered portion of the Main Bifurcated Stent-Graft that was identified at 24 months. A retrospective analysis of the 12-month imaging showed the presence of the fracture initially at 12 months. There is no evidence of clinical sequelae or migration, and the stent-graft remains patent. The maximum aneurysm diameter also remained stable through 12 months.* *[e] Patient experienced Type Ia endoleak 44 days post-implantation. This endoleak was sealed with a non-TREO device. A Type II endoleak was detected at the 6-month follow-up and confirmed resolved by the Core Laboratory at 12 months. This patient experienced a bare stent strut fracture in the proximal aspect of the uncovered portion of the Main Bifurcated Stent-Graft at 6 months. There is no evidence of clinical sequelae or migration, and the graft remains patent. The maximum aneurysm diameter also remained stable through 12 months.* *[f] Patient experienced a single barb break on the left side of the anterior aspect of the top stent at 36 months. A retrospective analysis of the 12-month imaging showed presence of the barb initially at 12 months. There have been no reported clinical sequelae through the patient's last visit at 60 months, and no evidence of endoleak, aneurysm sac expansion, patency compromise, or migration.* *[g] Patient experienced a single barb break at the left side of the anterior aspect of the bare proximal stent at 36 months. A retrospective analysis of the 12-month imaging showed presence of the barb initially at 12 months. There have been no reported clinical sequelae through the patient's last visit at 48 months, and no evidence of endoleak, aneurysm sac expansion, patency compromise, or migration.* *[h] Patient experienced Type Ib endoleak at 6 months only. No evidence of endoleak at 30 days, 12 months, 24 months, or 36 months.* *[i] Patient experienced Type II endoleak at 39 days, which was classified as Type Ia at 6 months and 12 months.*	

2.2 Secondary Effectiveness Endpoints

A summary of the secondary effectiveness endpoints through 4 years is presented in **Table 25** and summarized in the respective sections. The data presented are the number of patients with the event observed during each timepoint.

At 30-days, the technical success rate, defined as a patent endovascular graft, with an absence of Type I/III endoleak, or treated aneurysm sac rupture at 30 days confirmed by an imaging modality, was 98%. There were three device-related events: a Type Ia endoleak and two Leg Extension occlusions requiring intervention. There were no instances of aneurysm-related mortality, rupture, stent fracture or conversion to open surgery.

At 6-months, there were two Type 1a endoleaks reported and one Type Ib endoleak. Three additional interventions (two of which were re-interventions) also occurred.

One patient experienced a single stent strut fracture. There were no instances of aneurysm-related mortality, migration, aneurysm sac increase, rupture or conversion to open surgery.

At 1 year, there were two patients with one stent strut fracture and there were two patients with one barb fracture reported (including previously identified patients) but no clinical sequelae associated with the fractures. One patient experienced a Type 1a endoleak at the 1-month follow-up that was resolved with a non-TREO proximal cuff and adjunctive endostapling. No fracture was observed with this patient at the 1-month follow-up where the Type I endoleak was treated. Upon review of the 6-month follow-up imaging, the laser cut bare stent strut fracture was observed, although the Type I endoleak remained resolved. For all patients, there were no instances of aneurysm-related mortality, migration, aneurysm sac increase, rupture or conversion to open surgery.

At 2 years, there were three patients reported with one stent strut fracture and two patients reported with one barb fracture reported (including previously identified patients) but no clinical sequelae associated with the fractures. There was one Type Ia endoleak observed and was treated with a non-TREO proximal cuff. For all patients, there were no instances of aneurysm-related mortality, rupture, migration, aneurysm expansion, occlusions requiring intervention, or conversion to open surgery.

At 3 years, there were four patients reported with stent strut fractures, and three patients with one barb fracture reported (including previously identified patients) but no clinical sequelae associated with the fractures. One patient previously reported with a stent strut fracture at 2 years had a second stent strut fracture reported. There was one Type Ia endoleak observed and is being followed. Five patients were reported with aneurysm expansion, which was likely attributed to Type II endoleaks. For all patients, there were no instances of aneurysm-related mortality, rupture, migration, occlusions requiring intervention, or conversion to open surgery.

At 4 years, there were three patients reported with a single stent strut fracture, and three patients with a single barb fracture reported (including previously identified patients) but no clinical sequelae associated with the fractures. There were no Type I or III endoleaks reported. Aneurysm expansion was reported in three patients: two ongoing from prior timepoints and one new expansion which was likely attributed to Type II endoleak. For all patients, there were no instances of aneurysm-related mortality, rupture, migration, occlusions requiring intervention, or conversion to open surgery.

Table 25. Summary of Secondary Effectiveness Endpoints

Secondary Effectiveness Endpoints‡	Procedure	30 Days	6 Months	1 Year	2 Years	3 Years	4 Years
Technical Success	NA	98.0% (144/147)	NA	NA	NA	NA	NA
Major Device-Related Events	NA	2.0% (3/150)	3.6% (5/139)	3.6% (5/137)	5.2% (6/116)	14.1% (13/92)	28.1% (9/32)
Stent-Strut Fractures*	NA	0% (0/148)	0.8% (1/133)	1.5% (2/131)	2.7% (3/110)	4.7% (4/86)	10.0%§ (3/30)
Barb Fracture*	NA	0% (0/148)	0% (0/133)	1.5% (2/131)	1.8% (2/110)	3.5% (3/86)	10.0%§ (3/30)
Migration*	NA	NA	0% (0/134)	0% (0/128)	0% (0/111)	0% (0/91)	0% (0/28)
All Endoleaks*	0% (0/150)	24.7% (36/146)	18.7% (25/134)	17.3% (23/133)	13.3% (15/113)	10.6% (10/94)	9.4% (3/31)
Type Ia	0% (0/150)	0.7% (1/146)	1.5% (2/134)	0.8% (1/133)	0.9% (1/113)	1.1% (1/94)	0% (0/31)
Type Ib	0% (0/150)	0% (0/146)	0.7% (1/134)	0% (0/133)	0% (0/113)	0% (0/94)	0% (0/31)
Type II	0% (0/150)	23.3% (34/146)	17.2% (23/134)	15.0% (20/133)	11.5% (13/113)	9.6% (9/94)	9.4% (3/31)
Type III	0% (0/150)	0% (0/146)	0% (0/134)	0% (0/133)	0% (0/113)	0% (0/94)	0% (0/31)
Type IV	0% (0/150)	0% (0/146)	0% (0/134)	0% (0/133)	0% (0/113)	0% (0/94)	0% (0/31)
Unknown	0% (0/150)	0.7% (1/146)	0% (0/134)	1.5% (2/133)	0.9% (1/113)	0% (0/94)	0% (0/31)
Aneurysm Enlargement*	NA	NA	0% (0/137)	0% (0/136)	0% (0/116)	5.3% (5/94)	3.30% (3/30)
Occlusion Requiring Intervention	0% (0/150)	1.3% (2/148)	6.9% (1/145)	0% (0/138)	0% (0/122)	0% (0/91)	0% (0/28)
Conversion to Open Repair	0% (0/150)	0% (0/150)	0% (0/149)	0% (0/144)	0% (0/132)	0% (0/120)	0% (0/69)
Any Secondary Intervention	NA	4.7% (7/150)	2.0% (3/149)	0.7% (1/144)	2.3% (3/132)	1.7% (2/120)	0% (0/69)

All values expressed as % (n/N) for endpoints reported within the specified window.

*Denominators are specified in **Table 8** (Summary of Compliance and Imaging Follow-Up: Pivotal Study). For imaging endpoints (fractures, migration, endoleak, aneurysm enlargement), the denominator is the number of patients with imaging adequate to assess the parameter. For clinical endpoints (occlusion requiring intervention, conversion to open repair, secondary interventions), the denominator is the number of patients with visits within the window).*

Major device-related events are defined as those events comprising the primary effectiveness endpoint (fracture, migration, Type I/III endoleaks, aneurysm enlargement, occlusion requiring intervention, conversion to open repair).

**This data represents Core Laboratory assessed endpoint for any reports of fracture, migration, endoleak or aneurysm enlargement at each interval, including events previously identified at earlier intervals that are considered ongoing or persistent.*

‡For consistency, the cutoff for all data presented in this table is February 14, 2019, the initial PMA datacut. Information on events occurring after this datacut are presented in subsequent sections as appropriate.

Table 25. Summary of Secondary Effectiveness Endpoints

Secondary Effectiveness Endpoints‡	Procedure	30 Days	6 Months	1 Year	2 Years	3 Years	4 Years
§Section 6.4.19 Stent Graft Integrity includes additional longer-term data on barb and strut fractures. The stent-strut fracture rate at 4 years based on these data are 5.1% (3/59) and the barb break rate at 4 years was 6.8% (4/59). Not all patients with previously identified fracture have reached the 4-year interval at the time of data lock.							

2.2.1 Technical Success at 30 Days

Technical success at 30 days was defined as a patent endovascular graft, with an absence of Type I/III endoleak, or treated aneurysm sac rupture at 30 days confirmed by an imaging modality. While Technical Success at the index procedure is a component of the primary effectiveness endpoint, Technical Success at 30 days is a prespecified secondary endpoint. Technical success was 98.0% (144/147) in the Pivotal Study. There were 2 endovascular graft occlusions with reinterventions within 30 days and one Type Ib endoleak.

2.2.2 Device Assessment at Index Procedure

An Investigator assessment of device performance at the index procedure was also completed. Among the 150 patients in the Pivotal Study, the Investigator judged device delivery, deployment, patency, and integrity acceptable in all but one patient (149/150, 99.3%). This patient had unsatisfactory stent-graft deployment from the introducer sheath, but achieved satisfactory lesion exclusion. This did not count against the 30-day Technical Success endpoint since this was not confirmed on imaging studies.

2.2.3 Aneurysm-Related Mortality

There was no aneurysm-related mortality in patients enrolled in the Pivotal Study

2.2.4 Aneurysm Sac Rupture

There were no aneurysm ruptures in patients enrolled in the Pivotal Study

2.2.5 Migration

Migration in the Pivotal Study was defined as movement greater than 10 mm compared to the 1-month imaging. Through 4 years, no stent-graft migration was observed in study (**Table 26**). In addition, one patient completed 5-year follow-up and no migration was observed. Clinically significant migration is defined as when a secondary intervention is completed to address migration whether or not the migration reached the > 10 mm threshold. No clinically significant migration has been observed in the study.

Component separation between the Main Bifurcated Stent-Graft and Leg Extensions was not observed in the study.

Table 26. Summary of Core Laboratory Assessed Stent-Graft Migration (> 10 mm)

	6 months	12 months	2 years	3 years	4 years
# of patients eligible	134	128	111	91	28
Stent-Graft Migration (> 10 mm)	0	0	0	0	0
Clinically Significant Migration	0	0	0	0	0

2.2.6 Endoleaks

A summary of post-procedure endoleaks is provided in **Table 27**. Endoleaks were assessed by the Core Laboratory through follow-up. The majority were classified by the Imaging Core Laboratory as Type II. At the 30-day visit, 34 patients had confirmed Type II endoleaks, with half persisting through the 6-month visit.

Four patients (2.7%) developed a Type Ia endoleak over follow-up to date. One patient developed a Type Ia endoleak 44 days post implant, which was excluded with a non-TREO device. This patient did experience a bare stent fracture in the proximal aspect of the uncovered portion of the main body stent at 6 months. There was no evidence of clinical sequelae or migration, and the graft remained patent. The maximum aneurysm diameter remained stable through 12 months, after which the patient withdrew from study participation. One patient had a Type Ia at 6 months which the investigator elected not to treat. Two patients experienced Type Ia endoleaks during later follow-up: one at 2 years, which was treated with a non-TREO proximal cuff, and one at 3-year follow-up that is currently being followed. One patient developed a Type Ib endoleak at 6 months which resolved without additional intervention by 12-months.

There were no Type III or Type IV endoleaks observed by the Imaging Core Laboratory. Endoleaks that were determined by the Imaging Core Laboratory to have continued from one study visit to the next were captured as persistent.
One patient has completed 5-year follow-up and no endoleaks of any type were observed.

Table 27. Summary of Core Laboratory Reported Endoleaks

Endoleak	30 Days	6 Months	12 Months	2 Years	3 Years	4 Years
Adequate Imaging*	146	134	133	113	94	31
Endoleaks (Total)**	36 (24.7%)	25 (18.7%)	23 (17.3%)	15 (13.3%)	10 (10.6%)	3 (9.4%)
Type Ia						
New	1[a]	1[b]	0	1[c]	1[d]	0
Persistent	0	1	1	0	0	0
New and Persistent	1 (0.7%)	2 (1.5%)	1 (0.8%)	1 (0.9%)	1 (1.1%)	0 (0.0%)

Table 27. Summary of Core Laboratory Reported Endoleaks

Endoleak	30 Days	6 Months	12 Months	2 Years	3 Years	4 Years
Type Ib						
New	0	1[e]	0	0	0	0
Persistent	0	0	0	0	0	0
New and Persistent	0 (0.0%)	1 (0.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Type II						
New	34	6	4	1	2	1
Persistent	0	17	16	12	7	2
New and Persistent	34 (23.3%)	23 (17.2%)	20 (15.0%)	13 (11.5%)	9 (9.6%)	3 (9.4%)
Type III						
New	0	0	0	0	0	0
Persistent	0	0	0	0	0	0
New and Persistent	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Type IV						
New	0	0	0	0	0	0
Persistent	0	0	0	0	0	0
New and Persistent	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Unknown Type						
New	1	0	2	0	0	0
Persistent	0	0	0	1	0	0
New and Persistent	1 (0.7%)	0 (0.0%)	2 (1.5%)	1 (0.9%)	0 (0.0%)	0 (0.0%)

** Adequate imaging was determined by the Core Laboratory. In general, images with contrast and non-contrast series were regarded as adequate for interpretation of endoleaks.*
*** Endoleaks (Total) reflects the number of patients experiencing at least one endoleak of any type at the timepoint. One patient experienced two endoleaks at 6 months.*
[a] *Patient experienced Type Ia endoleak at 30 days. Classified as Type II at 6 months and resolved at 12-month follow-up visit.*
[b] *Patient experienced Type II endoleak at 39 days but classified as Type Ia at 6 months and 12 months.*
[c] *Patient experienced Type Ia endoleak at 2-year follow-up, which was then reported as a Type II at 3 years.*
[d] *Patient experienced Type Ia endoleak at 3-year follow-up, which is currently being followed. Patient had Type II lumbar endoleak reported at 30 days, which has persisted through 3 years.*
[e] *Patient experienced Type Ib endoleak at 6 months only (resolved without intervention by 12 months), and a Type II at 12 months. No evidence of endoleak at 30 days, 2 years or 3 years.*

2.2.7 Aneurysm Enlargement

Aneurysm enlargement was defined as an increase in aneurysm sac diameter greater than 5 mm relative to the diameter determined at the 1-month baseline evaluation. Aneurysm size changes for the study are summarized in **Table 28.** Aneurysm size changes were assessed by the Core Laboratory. In the Pivotal Study, 46.3% (63/136) of patients had >5 mm of sac regression at 12 months, and over 50% of patients had regression at years 2 through 4. Sac expansion was observed in 5/94 patients (5.3%) followed to 3 years, and 3/30 (10%) followed to 4 years (1 new

expansion & 2 perisisting expansions at 4 years). One patient completed 5-year follow-up and a stable aneurysm diameter was observed.

All patients with reported aneurysm sac expansion had previously reported Type II endoleaks, which may have contributed to the expansion. No other contributing factors were identified.

Table 28. Summary of Core Laboratory Assessed Changes in Aneurysm Sac Diameter

Changes in Aneurysm Size	6 Months	12 Months	2 Years	3 Years	4 Years
Imaging Adequate to Assess Diameter Change	100% (137/137)	100% (136/136)	100% (116/116)	100% (94/94)	100% (30/30)
Increase > 5mm					
New	0% (0/137)	0% (0/136)	0% (0/116)	5.3% (5/94)	3.3% (1/30)
Persistent	0% (0/137)	0% (0/136)	0% (0/116)	0% (0/94)	6.7% (2/30)
Total (New and Persistent)	0% (0/137)	0% (0/136)	0% (0/116)	5.3% (5/94)	10.0% (3/30)
No Change Total	68.6% (94/137)	53.7% (73/136)	45.7% (53/116)	40.4% (38/94)	36.7% (11/30)
Decrease (>5 mm)	31.4% (43/137)	46.3% (63/136)	54.3% (63/116)	54.3% (51/94)	53.3% (16/30)
All values expressed as % (n/N)					

2.2.8 Stent-Graft Integrity

Fracture was defined as any breakage of a metallic component of the Stent-Graft. The TREO is comprised of metallic components that are manufactured from either laser cut tubing or shape set wire. No shape set wire components exhibited fractures. The fractures reported were located in the bare stent component that is manufactured from laser cut tubing. Therefore, no fractures were identified in areas where the stents were connected to the fabric. Fractures of the bare stent were located in one of three areas: a suprarenal barb, the proximal end of a transrenal strut or the distal end of transrenal strut. In all cases of fracture, all portions of the metallic component were accounted for.

Incidence of the barb and stent strut fractures observed in 10 patients from the initial data-cut for the PMA are presented in **Table 25**. A comprehensive summary of observed fracture through 5 years is presented in **Table 29** and includes available data on fractures observed in 13 patients through January 2020, inclusive of outcomes of Core Laboratory re-review.

Stent fractures were reported by the Core Laboratory based on the images received from each site. Upon review of patient images by the Core Laboratory, 4 patients have been identified with 1 fracture each in a suprarenal barb. Two patients with a

barb fracture were first observed with fracture at 1 year, 1 patient at 2 years, and 1 patient at 3 years.

Nine different patients have been identified with a total of 13 stent strut fractures in the bare proximal stent (8 patients with fracture in the Main Bifurcated Stent-Graft, 1 patient with fracture in the Proximal Cuff Stent-Graft). One patient with stent strut fracture was reported at 6 months, 1 patient was reported with a new fracture at 1 year, 2 patients at 2 years, 1 patient at 3 years, 3 patients at 4 years, and 1 patient at 5 years. Only two of these 9 patients with stent strut fracture(s) have been observed with multiple fractures (1 patient with 2 stent strut fractures and one patient with 4 stent strut fractures), as presented in **Table 30**.

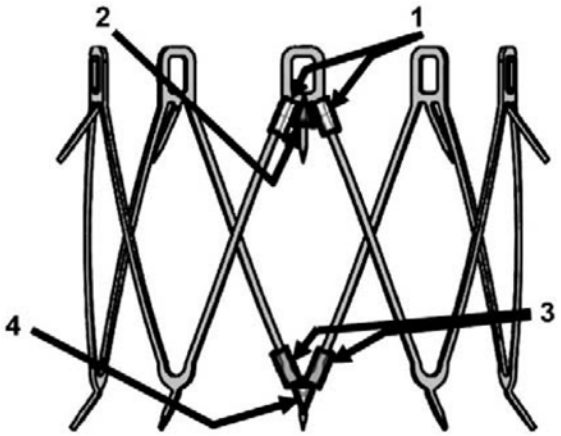
Table 29. Fracture Incidence and Prevalence Summary

	1 Month	**6 Months**	**1 Year**	**2 Years**	**3 Years**	**4 Years**	**5 Years**
Strut Fracture							
# of Patients Newly Identified with at Least 1 Strut Fracture[a]	0/148	1/133	1/131	2/111	1/94	3/59	1/22
Cumulative # of Patients with a Strut Fracture[b]	0	1	2	4	5	8	9
Cumulative # of Strut Fractures[c]	0	1	2	4	8	11	13
Barb Fracture							
# of Patients Newly Identified with at Least 1 Barb Fracture[a]	0/148	0/133	2/131	1/111	1/94	0/59	0/22
Cumulative # of Patients with a Barb Fracture[b]	0	0	2	3	4	4	4
Cumulative # of Barb Fractures[c]	0	0	2	3	4	4	4

[a] Newly identified patients with fracture at identified timepoint / number of patients at timepoint with imaging adequate to assess fracture through January 2020.
[b] Patients with fracture continue to be reported for later timepoints, regardless if they have reached the follow-up window.
[c] Number of fractures continue to be reported for later timepoints.

All fractures that have been reported in the TREO Pivotal Study have been observed in the bare proximal stent. For eight of the patients with stent strut fracture, the fracture was located on the bare proximal stent of the Main Bifurcated Stent-Graft. For one of the patients with strut fracture, the fracture was located on the bare proximal stent of the Proximal Cuff Stent-Graft. Of note, the proximal end of the Main Bifurcated Stent-Graft and the Proximal Cuff Stent-Graft (i.e., bare proximal stents) are identical. For the patients with stent strut fracture(s), the fracture(s) have been observed near the eyelet (9 fractures in 7 patients) and the distal strut (4 fractures in 3 patients). For the patients with a single barb fracture, the fracture was observed in the suprarenal barbs of the bare proximal stent of the Main Bifurcated Stent-Graft. No fractures have been observed in the infrarenal barbs. A single patient has been reported with both a fracture in the eyelet and also in the distal

strut. No patient has been reported with both a barb fracture and a strut fracture. See **Figure 7** below for depiction of these fracture locations.



Fracture Location Description / Summary		
1	Proximal Strut	7 Patients 9 Fractures[1]
2	Proximal Barb	4 Patients 4 Fractures
3	Distal Strut	3 Patients[1] 4 Fractures
4	Distal Barb	0 Fractures

[1]One patient had both a proximal and distal strut fracture and is counted at each location.

Figure 7: TREO Proximal Bare Stent Fracture Locations

Two patients have been reported with multiple stent strut fractures. Patient #1 was observed with 3 fractures at 36 months and 1 additional fracture reported at 60 months. Patient #2 was observed with 1 fracture at 24 months and 1 additional fracture at 36 months. All fractures have occurred in the bare proximal stent. **Table 30** below presents the fractures newly identified for these two patients at each follow-up visit.

Table 30. Patients with Multiple Stent Fractures at Follow-Up

Patient	1 Month	6 Months	1 Year	2 Years	3 Years	4 Years	5 Years
Patient #1	0	0	0	0	3	0	1
Patient #2	0	0	0	1	1	0	0

None of the patients with fracture have had clinical sequelae associated with fracture. This includes no observations of implant migration, Type Ia endoleaks, aneurysm enlargement, embolization of stent strut or barb segments, vessel perforation, aortic rupture, or secondary interventions required as a result of the fractures or death attributed to stent strut or barb fracture.

A root cause investigation was conducted regarding the observation of fracture. This investigation included patient anatomical data analysis, bench top testing of acute performance characteristics in observed and beyond observed fault conditions, in-vivo deformation analysis, computational strain simulations, and experimental fatigue testing. High axial drag forces and minimal barb penetration were identified as potential contributing causes of fracture. The information from the root cause investigation could not be correlated to any patient anatomical,

demographic, or procedural related factors that may contribute to an increased risk of fracture (for detailed description, see Section IX.A Fracture Root Cause Investigation).

2.2.9 Stent-Graft Patency-Related Events

Loss of stent-graft patency was defined as an occlusion where complete luminal obstruction of the Main Bifurcated Stent-Graft or one or both limbs of the stent-graft, leading to the absence of flow (i.e., loss of patency) across the involved segment/s was observed by the Core Laboratory. There were no Core Laboratory reports of patency issues (**Table 31)** involving full occlusion of the Main Bifurcated Stent-Graft and/or Leg Extension Stent-Grafts in the study, beyond events which were recognized clinically. Site-reported patency issues are described in **Table 32**.

As reported by the investigational sites, occlusion of a single Leg Extension Stent-Graft requiring intervention occurred in 3/150 (2%) patients. Among these, 2/150 occurred within 30 days, both of which were treated with secondary interventions. There was one additional occlusion requiring an intervention which occurred during the 6 months timepoint. All occlusions were of the Leg Extensions; there were no occlusions of the Main Bifurcated Stent-Graft.

Table 31. Core Laboratory Reported Stent Graft Patency

Patency	30 Days	6 Months	12 Months	2 Years	3 Years	4 Years
Pivotal	100% (147/147)	100% (134/134)	100% (134/134)	100% (113/113)	100% (66/66)	100.0% (12/12)
Core Laboratory-reported. This data may differ from the site-reported data if an occlusion was treated such that the endograft was patent later, on the image submitted to the Core Laboratory for protocol-defined follow-ups.						

Table 32. Summary of Site-Reported Stent Graft Occlusion

Interval	Eligible Patients	New Occlusions	Persistent Occlusions	Cumulative Secondary Procedures*
Procedure	150	0	0	0
30 Days	148	2[a,b]	0	2
6 Months	145	1[c]	0	3
12 Months	138	0	0	3
2 Years	144	0	0	3
3 Years	91	0	0	3
4 Years	28	0	0	3
5 Years	0	0	0	3

Table 32. Summary of Site-Reported Stent Graft Occlusion

Interval	Eligible Patients	New Occlusions	Persistent Occlusions	Cumulative Secondary Procedures*

** Secondary Procedures that successfully restored patency. There were no unsuccessful secondary procedures in the study*

[a] Patient 423-116 experienced stent occlusion of the left proximal iliac artery, which was successfully treated 9 days post-implant with angioplasty and embolectomy. Patient's medical history was significant for peripheral vascular disease and extensive atherosclerotic vascular disease, with a narrow distal aortic neck. There were no other site-reported contributing factors related to this thrombosis event.

[b] Patient 418-110 experienced occlusion of the right iliac Leg Extension, which was initially treated 30 days post-implant with lytic therapy, PTA of thrombosis, and angioplasty of right iliac. Patient was then treated the following day (31 days post-implant) with endovascular revascularization and open right iliac with non-TREO stents and angioplasty, which resolved the occlusion. There were no site-reported contributing factors related to this thrombosis event.

[c] Patient 401-103 experienced occlusion of the right iliac Leg Extension, which was treated 12 days post-implant with right common femoral endarterectomy with patch arthroplasty, right common iliac stent with angioplasty, and right common iliac embolectomy. This treatment did not resolve the occlusion, and 79 days post-index procedure patient was successfully treated with left to right femoral to femoral bypass, right proximal superficial femoral artery stent x 2, and right distal superficial femoral artery stent x 2. Patient's medical history was significant for aneurysmal right and left common iliac arteries, left lower extremity peripheral vascular disease status post thrombectomy, and PTA and SFA stenting in 2004. Per the Operative Report, the patient's pre-implant imaging was significant for right hypogastric artery coiling, and patient had moderate to severe disease distal to the external iliac artery. There were no other site-reported contributing factors related to this thrombosis event.

The Core Laboratory assessed kinking of the stent graft. Kinking of the stent graft was reported in one patient at the time of the index procedure (0.7% of 149 patients with data reported). This event was not site-reported, and no loss of patency or clinical sequelae were noted at any follow-up visits to date and no reintervention was required. No stent graft kinks were reported in follow-up thereafter.

2.2.10 Conversion to Open Surgery

There were no open surgical conversions in the study.

2.2.11 Secondary Interventions

There have been a total of 18 secondary interventions performed in 16 patients through 4 years in the TREO Pivotal Study. The majority of interventions were performed to address patency-related events and endoleaks. Three patients were treated for implant occlusion, and an additional five patients received treatment for thrombus, ischemia, stenoses and one was treated for AV fistula. One patient who experienced aneurysm sac expansion underwent embolization due to a persistent Type II endoleak. One patient followed through 5 years has no reported secondary interventions. A summary of the reasons for secondary interventions are shown in **Table 33**. Narratives on each intervention are provided in the footnotes**.**

Table 33. Summary of Reasons for Secondary Intervention

	30 Days	6 Months	1 Year	2 Years	3 Years	4 Years
Number of Patients Eligible (at Risk)	150	149	144	132	120	69
Patients with Any Intervention	7 4.7% (7/150)	3 2.0% (3/149)	1 0.7% (1/144)	3 2.3% (3/132)	2 1.7% (2/120)	0 0% (0/69)
Number of Interventions	8	4	1	3	2	0
Secondary Intervention for Type I Endoleak	1 (1) 0.7% (1/150)	3 (3) 2.0% (3/149)	1 (1) 0.7% (1/144)	1 (1) 0.8% (1/132)	0 (0) 0% (0/120)	0 (0) 0% (0/69)
Extension	1[a]	3[b, c, d]	0[d]	1[e]	0	0
Secondary Intervention for Type II Endoleak	0 (0) 0% (0/150)	0 (0) 0% (0/149)	0 (0) 0% (0/144)	1 (1) 0.8% (1/132)	1 (1) 0.8% (1/120)	0 (0) 0% (0/69)
Coil Embolization	0	0	0	1[f]	1[g]	0
Secondary Intervention for Implant Occlusion	3 (3) 2.0% (3/150)	0 (0) 0% (0/149)	0 (0) 0% (0/144)	0 (0) 0% (0/132)	0 (0) 0% (0/120)	0 (0) 0% (0/69)
Endarterectomy, Arthroplasty, and Embolectomy	1[h]	0	0	0	0	0
Angioplasty, Embolectomy and Stenting	2[i, j]	0	0	0	0	0
Secondary Intervention for Aneurysm Sac Expansion	0 (0) 0% (0/150)	0 (0) 0% (0/149)	0 (0) 0% (0/144)	1 (1) 0.8% (1/132)	0 (0) 0% (0/120)	0 (0) 0% (0/69)
Embolization	0	0	0	1[k]	0	0
Secondary Intervention for Thrombus	1 (1) 0.7% (1/150)	0 (0) 0% (0/149)	0 (0) 0% (0/144)	1 (1) 0.8% (1/132)	1 (1) 0.8% (1/120)	0 (0) 0% (0/69)
Embolectomy	1[l]	0	0	0	1[n]	0
Embolectomy and Extension	0	0	0	1[m]	0	0
Secondary Intervention for Ischemia	1 (1) 0.7% (1/150)	1 (1) 0.7% (1/149)	0 (0) 0% (0/144)	0 (0) 0% (0/132)	0 (0) 0% (0/120)	0 (0) 0% (0/69)
Extension	1[o]	1[c]	0	0	0	0
Secondary Intervention for AV Fistula	1 (1) 0.7% (1/150)	0 (0) 0% (0/149)	0 (0) 0% (0/144)	0 (0) 0% (0/132)	0 (0) 0% (0/120)	0 (0) 0% (0/69)
Extension	1[p]	0	0	0	0	0

Where n(n) is number of patients with an event (number of events) and N is the number of patients with visits in the specified window.

[a] *One patient presented with a Type I endoleak 44 days post-implantation, which was treated with a non-TREO aortic cuff. A Type II endoleak was detected at the 6-month follow-up but confirmed resolved by the Core Laboratory at 12 months. This patient experienced a wireform fracture in the proximal aspect of the uncovered portion of the Main Bifurcated Stent-Graft at 6 months. There is no evidence of clinical sequelae or migration, and the graft remains patent. The maximum aneurysm diameter remained stable through 12 months.*

[b] *One patient was reported by the site to have a Type Ia endoleak; however, this was not confirmed by the Imaging Core Laboratory and is therefore not reported as such elsewhere in this report. Per the Imaging Core Laboratory, there was no evidence of endoleak of any type upon completion angiogram for this patient. At the 30-day follow-up, a Type II endoleak was detected by the Imaging Core Lab (as opposed to a Type Ia). This endoleak was confirmed by the Imaging Core Laboratory to persist at the 6-month and 12-month follow-up visits and had resolved by the 2-year follow-up visit. The endoleak and non-occlusive thrombus in the right limb was treated with the implantation of another TREO device during a secondary intervention at 169 days post-implant procedure. This patient also had an embolectomy at 1141 days post-implant for recurrence of non-occlusive thrombus.*

[c] *One patient underwent a secondary intervention 231 days post-implant to address a Type Ib endoleak by placement of an extension. Shortly thereafter, on day 265 post-implant, the patient developed severe right leg ischemia and underwent an additional procedure the following day to address the ischemia. A non-TREO stent was placed in the right iliac, resolving the ischemia.*

[d] *One patient experienced a Type II endoleak at 39 days, which was not present on the completion angiogram. The patient then experienced a Type Ia endoleak at 6 months and 12 months, which was treated with a competitor's device placed within the TREO stent-graft on day 265 post-implant, and later a coil embolization on day 390 post-implant.*

[e] *One patient experienced a Type Ia endoleak at the 2-year follow-up. On day 870 post-implant, the patient had a competitor extension implanted.*

[f] *One patient had a Core Laboratory-determined maximum aneurysm diameter of 59.7mm at 1-month follow-up, which was stable at 60.9mm through 24 months. The site-reported 1-month aneurysm diameter was 55mm; smaller than the Core Lab. At 24 months, the site-reported aneurysm diameter increased to 63mm; an 8mm increase compared to the 1-month site measurement. A Type II endoleak, first noted at 1 month, was embolized. Following embolization (27 months), maximum aneurysm diameter was 73mm (+13.3mm compared to 1-month image, Core Lab measurements). The maximum diameter of the aneurysm decreased to 69.2mm (+9.5mm) at 36 months, without a detectable endoleak reported at that time. The aneurysm continued to decrease to 67.1 (+7.4) at 48 months.*

[g] *One patient experienced a Type II endoleak that had persisted since implant and was treated with embolization on days 1141 and 1148 post-implant. This patient had a maximum aneurysm diameter of 58.2mm at 1 month, which was stable through 24 months but increased to 63.9mm (+5.7mm) at 36 months, meeting the criteria for aneurysm sac increase. The diameter increased further to 68.8mm (+10.6mm) at 48 months.*

[h] *One patient experienced an occlusion of the right Leg Extension, which was treated 12 days post-implant with right common femoral endarterectomy with patch arthroplasty, right common iliac stent with angioplasty, and right common iliac embolectomy. This treatment did not resolve the occlusion, and 79 days post-index procedure patient was successfully treated with left to right femoral to femoral bypass, right proximal superficial femoral artery stent x 2, and right distal superficial femoral artery stent x 2.*

[i] *One patient experienced stent occlusion of the left proximal iliac artery, which was successfully treated 9 days post-implant with angioplasty and embolectomy.*

[j] *One patient experienced an occlusion of the right Leg Extension, which was initially treated 30 days post-implant with lytic therapy, PTA of thrombosis, and angioplasty of right iliac. Patient was then treated the following day (31 days post-implant) with endovascular revascularization and open right iliac with non-TREO stents and angioplasty, which resolved the occlusion.*

[k] *One patient had a Core Laboratory-determined maximum aneurysm diameter of 59.7mm at 1-month follow-up, which was stable at 60.9mm through 24 months. The site-reported 1-month aneurysm diameter was 55mm; smaller than the Core Laboratory. At 24 months, the site-reported aneurysm diameter increased to 63mm; an 8mm increase compared to the 1-month site measurement. A Type II endoleak, first noted at 1 month, was embolized. Following embolization (27 months), maximum aneurysm diameter was 73mm (+13.3mm compared to 1-month image, Core Lab measurements). The maximum diameter of the aneurysm decreased to 69.2mm (+9.5mm) at 36 months, without a detectable endoleak reported at that time. The aneurysm continued to decrease to 67.1 (+7.4) at 48 months.*

[l] *One patient experienced thrombosis in the right iliac one-day post-implant, which was corrected via embolectomy.*

[m] *One patient experienced thrombus in the left Leg Extension iliac limb 723 days post-implant. A non-TREO left iliac limb was deployed with successful results.*

[n] *One patient was reported by the site to have a Type Ia endoleak; however, this was not confirmed by the Imaging Core Laboratory and is therefore not reported as such elsewhere in this report. Per the Imaging Core Laboratory, there was no evidence of endoleak of any type upon completion angiogram for this patient. At the 30-day follow-up, a Type II endoleak was detected by the Imaging Core Laboratory (as opposed to a Type Ia). This endoleak was confirmed by the Imaging Core Laboratory to persist at the 6-month and 12-month follow-up visits and had resolved by the 2-year follow-up visit. The endoleak and non-occlusive thrombus in the right limb was treated with the implantation of another TREO device during a secondary intervention at 169 days post-implant procedure. This patient also had an embolectomy at 1141 days post-implant for recurrence of non-occlusive thrombus.*

[o] *One patient experienced right iliofemoral ischemia 11 days post-implant, which was successfully treated with a right iliofemoral embolectomy, PTA of bilateral iliac limbs, and stenting of the right CIA.*

[p] *One patient experienced a left groin av fistula 74 days post-implant, which was treated with a non-TREO covered stent, overlapping with the Leg Extension of the TREO device.*

2.2.12 Patient Accountability and Partial 5-year Follow-up Data

As of January 2020, 26 patients have completed five-year follow-up visits, of which 25 had CT imaging assessed by the imaging Core Laboratory, and 22 had x-ray imaging assessed. In addition, 74 patients have completed 4-

year follow-up and 107 patients have completed 3-year follow-up. Among the patients returning for follow-up since the initial PMA data-cut on February 14, 2019, there have been four deaths (one secondary to metastatic squamous cell carcinoma and three resulting from MI). Two patients have undergone secondary interventions (one for renal artery stenosis and the other to address a previously identified Type Ia endoleak that was contributing to aneurysm sac expansion at 4 years). Aneurysm sac increase was reported in three patients at 4 years and two patients through 5 years, all related to persistent Type II endoleaks. There have been no reports of migration, open surgical conversion, aneurysm rupture or aneurysm related mortality.

Since the 1-year follow-up timepoint, there have been an additional 9 patients with strut or barb fractures through partial 5-year follow-up. There continue to be no reports of clinical sequelae associated with fracture. Additional annual follow-up examinations through 10 years will continue for patients who experienced a stent-strut or barb fracture within the first 5 years of study participation.

3. Subgroup Analyses

No subgroup analyses were performed.

4. Pediatric Extrapolation

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

D. 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 154 investigators. None of the clinical investigators had disclosable financial interests/arrangements, as defined in sections 54.2(a), (b), (c), and (f). The information provided does not raise any questions about the reliability of the data.

XI. 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.

XII. CONCLUSIONS DRAWN FROM PRECLINICAL AND CLINICAL STUDIES

A. Effectiveness Conclusions

The primary effectiveness endpoint of successful aneurysm treatment was achieved in 93.13% of the TREO Pivotal Study cohort (122/131; 95% CI 87.36% to 96.81%, **Table 23**) through 12 months. The study did not meet the primary effectiveness endpoint as the lower confidence interval (i.e., 87.36%) was less than the effectiveness performance goal of 88% (P=0.0400). However, the performance goal for the primary effectiveness endpoint for this pivotal study was more conservative as compared to other endovascular graft pivotal studies evaluating similar intended patient populations. As described below, the rate of successful aneurysm treatment was clinically meaningful.

The technical success (intra-procedure) rate was 100%. Stent-grafts were patent at the end of the procedure in all patients. One patient had a Type Ia endoleak noted at the end of the index procedure, but this was not confirmed by the Imaging Core Laboratory and not present on the 30-day CT scan, so did not count against the effectiveness endpoint.

Overall, 9 patients did not meet the definition of treatment success based on observations through 12 months:

- Three Type I endoleaks reported by the Core Laboratory;
- Three endovascular graft occlusions requiring reintervention;
- Two patients each with 1 barb fracture, none of which were associated with clinical sequelae; and
- Two patients each with 1 stent strut fracture, none of which were associated with clinical sequelae.

One of the nine patients experienced two endpoint events: a Type Ia endoleak at 44 days and a stent fracture which was detected at the 6-month follow-up visit.

There were no reports of aneurysm-related mortality, rupture, conversion to open surgical repair, Type III endoleaks, or migration through 4 years.

The additional events reported after 12 months through 4 years include:

- Two patients each with 1 barb fracture, none of which were associated with clinical sequelae.
- Seven patients with stent strut fracture(s), none of which were associated with clinical sequelae.
    - One patient with 3 stent strut fractures at 3 years and an additional stent strut fracture identified at 5 years.
    - One patient with 1 stent strut fracture at 2 years and an additional stent strut fracture identified at 3 years.
    - All other patients had a single stent strut fracture observed.
- Six patients with aneurysm expansion (5 patients at 3 years, 1 new patient at 4 years), all associated with Type II endoleaks.
- Two patients with Type Ia endoleaks (1 patient at 2 years, 1 new patient at 3 years).

Throughout the study, there have been a total of 16 patients with 18 secondary interventions through 4 years. The majority of interventions were performed to address patency-related events and endoleaks.

Based on the clinical endpoint outcomes presented above, there is reasonable assurance of the effectiveness of the TREO for the proposed intended use.

B. Safety Conclusions

The risks of the device are based on nonclinical laboratory and animal, as well as data collected in a clinical study conducted to support PMA approval as described above.

The TREO Pivotal Study composite rate for MAE was 0.7% (1/150, 95% CI 0.0% to 3.7%) at 30 days. The upper bound of the 95% confidence interval of 3.7% is below the 19% performance goal indicating that the performance goal was met. One patient experienced procedural bleeding of 1000 mL and a myocardial infarction within the first 30 days.

The secondary endpoints of the study included MAEs and the individual components at 6 months and annually through 5 years. The MAE rate at each interval was less than 6.5%. Twenty-seven patients experienced 37 events. The most common event was death unrelated to the device or to the procedure, occurring in 18 patients through 4 years, none of which were aneurysm-related. Additional reported events include stroke (10 events), myocardial infarction (5 events), respiratory failure (2 events), and bowel ischemia (1 event). The safety outcomes are consistent with the safety outcomes reported in pivotal studies for AAA endovascular grafts. None of the events rates are unexpected.

The outcomes presented above demonstrate a reasonable assurance of safety of the TREO for the proposed intended use.

C. Benefit-Risk Determination

The probable benefits of the device are based on the data collected in a clinical study conducted to support PMA approval as described above. The TREO consists of standard endovascular graft technology, incorporating design features into device delivery, deployment, and withdrawal that are intended to improve ease of use and reduce vascular trauma. Additionally, the modular design includes a lock stent that is intended to reduce the risk of limb separation and Type IIIa endoleaks. TREO provides a small iliac limb profile option for physicians who prefer to utilize a traditional stent-graft for infrarenal abdominal aortic and aortoiliac aneurysm repair.

In the TREO Pivotal Study, there was no aneurysm-related mortality, aneurysm rupture, or conversion to open surgical repair. In addition, the majority of patients had aneurysms that decreased or remained stable in diameter during follow-up.

The probable risks of the device are also based on data collected in a clinical study conducted to support PMA approval as described above. The MAEs reported under this study are consistent with other studies of endovascular grafts to treat AAA. Device-related risks include aneurysm expansion, stent-graft occlusion, the need for secondary intervention and fracture of the bare proximal stent (barb and strut), as described above. Although there were more fractures observed in the Pivotal Study as compared to pivotal studies of some currently marketed endovascular grafts, none of the fractures were associated with clinical sequelae through partial 4-year follow-up.

In conclusion, given the available information above, the data support that, for the endovascular treatment of patients with infrarenal abdominal aortic and aorto-iliac aneurysms, the probable benefits outweigh the probable risks.

1. Patient Perspectives

This submission did not include specific information on patient perspectives for this device.

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 pre-clinical testing performed in accordance with applicable guidance documents and national and international standards confirmed that the TREO met its performance and design specifications. The primary safety endpoint was met. While the primary effectiveness endpoint did not meet the performance goal, the effectiveness-related outcomes were favorable and comparable to outcomes reported for pivotal studies of currently marketed endovascular grafts (i.e., 100% technical success rate and the 93.13% successful aneurysm treatment rate). The longer-term clinical data supports continued favorable safety and effectiveness-related outcomes. Patients are likely to benefit from the use of the TREO® Abdominal Stent-Graft in the endovascular repair of infrarenal abdominal aortic and aorto-iliac aneurysms.

XIII. CDRH DECISION

CDRH issued an approval order on May 4, 2020. The final conditions of approval cited in the approval order are described below.

Bolton has agreed to provide a Clinical Update to physician users at least annually. At a minimum, this update will include, for the IDE study cohort and post-approval study cohort, respectively, a summary of the number of patients for whom data are available, with the rates of major adverse events, aneurysm-related mortality, aneurysm rupture, secondary endovascular procedures, conversions to surgical repair, endoleaks, aneurysm enlargement, prosthesis migration, occlusions, stenoses, losses of device integrity, and other procedure or device-related events. Reasons for secondary interventions and conversion to open surgery as well as causes of aneurysm-related death and rupture are to be described. 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 and the information supporting the updates must be provided in the Annual Report.

In addition to the Annual Report requirements, Bolton has agreed to provide the following data in post-approval study (PAS) reports for each study listed below.

1. Continued Follow-up of the IDE Study Subjects: This is a prospective, single-arm, multi-center study that consists of continued follow-up of all available subjects from the IDE Pivotal and Continued Access studies. A total of 158 subjects were enrolled in the study and remaining subjects will be followed for 5 years, with the exception of subjects identified with fracture(s) within the first 5 years who will be followed for an additional 5 years (total of 10 years of follow-up). Secondary endpoints through 5 years (or 10 years for patients with fracture(s)) will include major adverse events, all-cause mortality, aneurysm-related mortality, aneurysm rupture, secondary interventions, conversion to open surgery, losses of device integrity, device occlusions, stenosis or kink, aneurysm enlargement (> 5 mm), stent graft migration (> 10 mm), all types of endoleaks, and other device-related events. No formal hypothesis testing will be performed for the longer-term follow-up. Outcomes will be reported using descriptive statistics annually.

2. TREO Post Approval Study: This is a prospective, multi-center, non-randomized, single arm, post approval study. The objective of the study is to collect confirmatory safety and effectiveness data of the TREO® Abdominal Stent-Graft System with emphasis on subjects that may experience a device strut or barb fracture in routine clinical practice. The study will prospectively enroll a minimum of 300 subjects at up to 40 U.S. sites. Follow-up will occur at 30 days, 1 year, and annually thereafter through 5 years. The primary endpoints are stent fracture, barb separation, and secondary intervention for adverse events related to stent fracture or barb separation. Additional endpoints will be collected and reported at each follow-up point through 5 years post-procedure, including but not limited to the following: technical success, major adverse events, all-cause mortality, aneurysm-related mortality, aneurysm rupture, secondary interventions, conversion to open surgery, losses of device integrity, device occlusions, stenosis or kink, aneurysm enlargement (> 5 mm), stent graft migration (> 10 mm), all types of endoleaks, and other device-related events. Outcomes will be reported using descriptive statistics every six months during the first two years of the study and annually thereafter.

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

XIV. 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.