SUMMARY OF SAFETY AND EFFECTIVENESS DATA (SSED)

I. GENERAL INFORMATION

Device Generic Name:	Stent Graft, Bypass, Superficial Femoral Artery
Device Trade Name:	DETOUR™ System
Device Procode:	QWM
Applicant's Name and Address:	Endologix LLC 2 Musick Irvine, CA 92618
Date(s) of Panel Recommendation:	None
Premarket Approval Application (PMA) Number:	P220021
Date of FDA Notice of Approval:	June 7, 2023

Breakthrough Device: Granted breakthrough device status on September 2, 2020 for percutaneous revascularization of symptomatic femoropopliteal lesions 200mm to 460mm with a chronic total occlusion 100mm to 425mm, and/or moderate-to-severe calcification, and/or in-stent-restenosis in patients with severe peripheral arterial disease.

II. INDICATIONS FOR USE

The DETOUR™ System is indicated for use for percutaneous revascularization in patients with symptomatic femoropopliteal lesions from 200mm to 460mm in length with chronic total occlusions (100mm to 425mm) or diffuse stenosis >70% who may be considered suboptimal candidates for surgical or alternative endovascular treatments. The DETOUR™ System, or any of its components, is not for use in the coronary and cerebral vasculature.

III. CONTRAINDICATIONS

The DETOUR™ System is contraindicated in patients with:

- A distal common femoral artery (CFA) <7 mm in diameter.
- Increased risk of deep vein thrombosis (DVT), such as patients with a recent history of DVT, thrombophilia, and disseminated malignancy.
- Untreated flow-limiting aortoiliac occlusive disease.
- Lack of patent single vessel tibial runoff to ankle.
- Known coagulopathy, bleeding diathesis, or thrombocytopenia that cannot be medically managed.
- Known hypersensitivities, allergies or contraindications to: Nitinol; PTFE; aspirin; heparin; antiplatelet; anticoagulant or thrombolytic therapy; or contrast media that cannot otherwise be medically managed.

IV. WARNINGS AND PRECAUTIONS

The warnings and precautions can be found in the DETOUR™ System labeling.

V. DEVICE DESCRIPTION

The DETOUR™ System is comprised of two (2) main components:

- TORUS™ Stent Graft System; comprised of the:
  - TORUS™ Stent Graft
  - TORUS™ Stent Graft Delivery System
- ENDOCROSS™ Device

TORUS Stent Graft System

The implantable TORUS Stent Graft (**Figure 1**) is a flexible, self-expanding composite structure made of a Nitinol (NiTi) wire frame encapsulated in an Expanded Polytetrafluoroethylene (ePTFE) film and Fluorinated Ethylene Propylene (FEP). The TORUS Stent Graft is pre-loaded onto the TORUS Stent Graft Delivery System.

Figure 1: TORUS Stent Graft

The TORUS Stent Graft is available in a variety of sizes outlined in **Table 1**. These can be deployed in a variety of configurations as outlined in **Table 2**.

Table 1: Vessel Diameter

Labeled Device Diameter (mm)	Reference Vessel Diameter (mm)	Available Device Nominal Lengths (mm)	Recommended Balloon Diameter for Post-Dilation (mm)
5.5	4.5-5.5	200	5.5
6.0	5.6-6.0	100, 150, 200	6.0
6.7	6.1-6.7	100, 150, 200	7.0

Table 2: Recommended Sizing Chart

Lesion Length (mm)	Number of Stent Grafts*	Stent Graft 1 Nominal Length (mm)	Stent Graft 2 Nominal Length (mm)	Stent Graft 3 Nominal Length (mm)
200-220	2	150	150	N/A
230-270	2	200	150	N/A
280-320	2	200	200	N/A
330-410	3	200	200	150
420-460	3	200	200	200

**60mm of stent graft overlap is required*

The TORUS Stent Graft Delivery System (**Figure 2**) is an 8 French (Fr) system. It is compatible with a 0.035" guidewire and has a 135 cm working length. The handle of the delivery system consists of an internal pulley mechanism activated through turning an external knob. The handle also features fluid flush ports for the inner lumen and guidewire lumen. The TORUS Stent Graft Delivery System uses an outer sheath to maintain the TORUS Stent Graft implant in a compressed state. Once at the target site, the user can slide the outer sheath proximally by turning the knob in the direction of the arrow to expose the self-expanding TORUS Stent Graft. The TORUS Stent Graft Delivery System has Platinum-Iridium (PtIr) radiopaque markers on both the proximal and distal ends of the TORUS Stent Graft landing zone (part of the inner shaft), and a marker band on the outer sheath to allow visualization of the position of the inner and outer sheath during deployment.

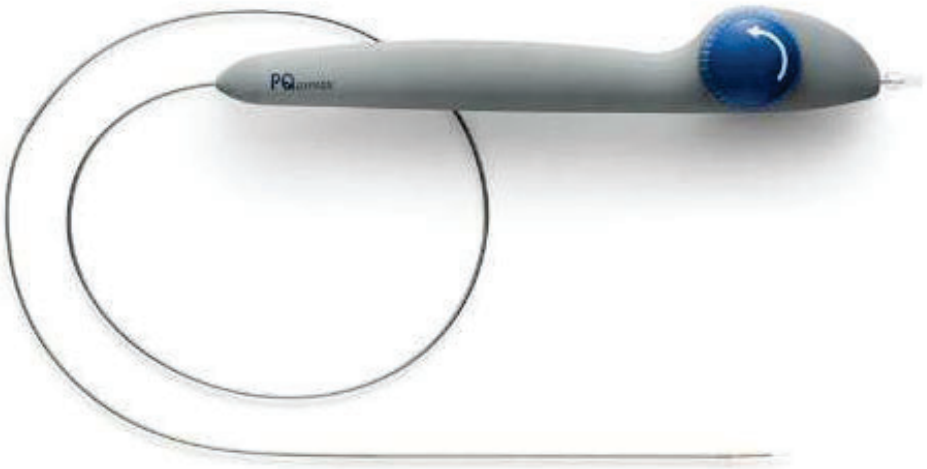

Figure 2: TORUS Stent Graft Delivery System

ENDOCROSS Device

The ENDOCROSS Device (**Figure 3**) is a dual guidewire delivery tool that uses a 0.025" Nitinol needle. The needle exits the delivery tool at an angle approximately 45° to the ENDOCROSS Device shaft. The ENDOCROSS Device is an 8 Fr compatible device with a

133 cm working length, dual 0.014” guidewire ports, a rapid exchange (RX) guidewire port, and a needle guidewire port. The RX guidewire port is a back-loaded, rapid-exchange design used for initial device placement. The needle guidewire port is the central lumen, and the lumen exits through the needle and is used to deliver guidewire(s) to the desired location. The ENDOCROSS Device features are controlled using the outer handle and the button on the ENDOCROSS Device handle.

The outer handle controls spring loading, stabilizer deployment, and needle activation. The user moves the handle slider proximal to distal, then rotates the handle counterclockwise to load the spring, deploy the stabilizer, and activate the needle for deployment in a single motion. The ENDOCROSS Device shaft is keyed to ensure that the needle deploys in the same orientation as the marker band. Subsequent depression of the handle button deploys the needle in the direction indicated by the marker band.

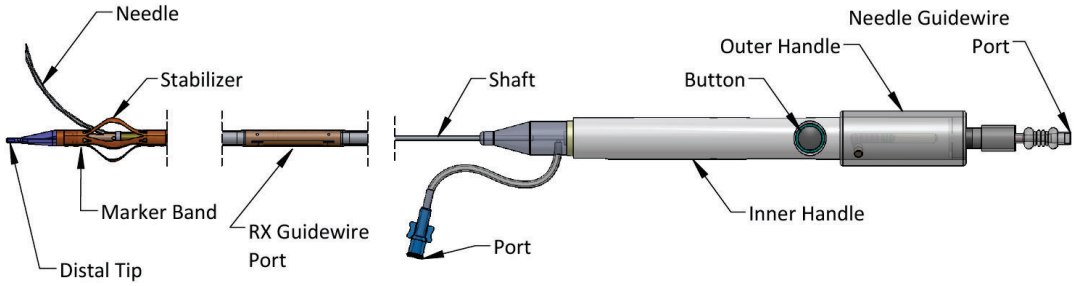

Figure 3: ENDOCROSS Device

Overview of the Procedure Using the DETOUR System

The procedure using the DETOUR System is an endovascular femoral-popliteal bypass procedure using the femoral vein as a conduit for the TORUS Stent Grafts which provides a bypass of the diseased arterial segment. Utilizing standard endovascular techniques, the ENDOCROSS Device is used to create an arterio-venous connection above the diseased arterial segment, and then a veno-arterial connection below the diseased arterial segment. TORUS Stent Grafts are then placed from distal to proximal sequentially to provide the bypass. Multiple TORUS Stent Grafts may be utilized during the procedure.

A graphical representation of the procedure using the DETOUR System is provided in (**Figure 4**).

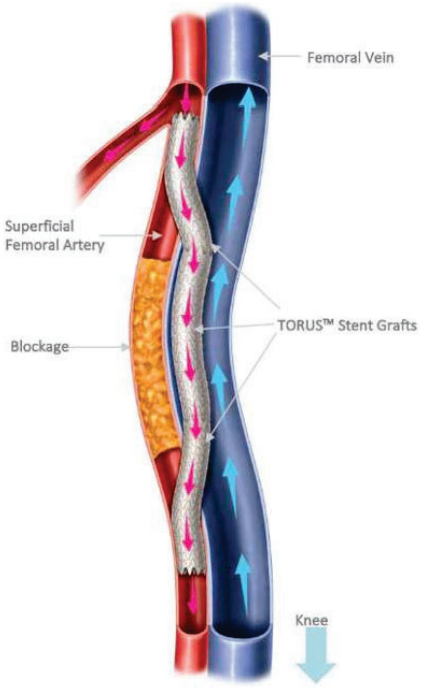

Figure 4: Procedure Utilizing the DETOUR System

VI. ALTERNATIVE PRACTICES AND PROCEDURES

There are several other alternatives for the correction of atherosclerotic disease of the superficial femoral and proximal popliteal arteries. Minimally-invasive approaches include endovascular intervention such as percutaneous transluminal angioplasty with a plain or drug-coated balloon, stent (e.g., bare metal, drug-eluting, or covered), and atherectomy. Surgical bypass procedures using autogenous or synthetic grafts are an option for long segment disease. 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 DETOUR System has been used in one (1) training case that was conducted outside of the clinical study. The training case was conducted in Germany while the device was CE Marked. The DETOUR System is no longer CE Marked and has not undergone full commercial launch in the United States or any foreign country.

VIII. POTENTIAL ADVERSE EFFECTS OF THE DEVICE ON HEALTH

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

- Access vessel (arterial / venous) occlusion
- Amputation
- Aneurysm or pseudoaneurysm

- Arteriovenous (AV) fistula
- Bleeding complications
- Death
- Device or deployment malfunction/failure
- Drug reactions to antiplatelet agents or contrast medium
- Edema
- Embolism (peripheral or pulmonary)
- Fever in absence of infection
- Hemorrhage or hematoma
- Hypotension / hypertension
- Infection (local or systemic including bacteremia or septicemia)
- Malposition
- Migration
- Myocardial infarction
- Pain (insertion site, leg and/or foot)
- Peripheral ischemia
- Renal insufficiency or failure secondary to contrast medium
- Shock
- Side branch vessel occlusion
- Stenosis or occlusion
- Stroke or transient ischemic attack
- Thrombosis
- Vessel wall trauma (dissection, perforation, or rupture)
- Vessel spasm
- Venous flow disruption (deep vein thrombosis, phlebitis, leg swelling and/or development of varicose veins)
- Worsening claudication

For the specific adverse events that occurred in the clinical study, please see Section D.1, Safety Results below.

IX. SUMMARY OF NONCLINICAL STUDIES

A. Laboratory Studies

The biocompatibility of the DETOUR System was evaluated per ISO 10993-1:2018 and FDA's Guidance for Industry and Food and Drug Administration Staff: *Use of International Standard ISO 10993-1, "Biological evaluation of medical devices – Part 1: Evaluation and testing within a risk management process"* (September 2020).

Tests were conducted separately on products manufactured, packaged, and sterilized using materials and procedures intended for the marketed product for the TORUS Stent Graft, TORUS Stent Graft Delivery System, and ENDOCROSS Device.

The TORUS Stent Graft is categorized as a permanent implant device that comes into contact with circulating blood (>30 days). The TORUS Stent Graft Delivery System and the ENDOCROSS Device are classified as externally communicating devices that come into contact with circulating blood for a limited duration (<24 hours). A summary of the biocompatibility testing conducted can be found in **Table 3** below.

Table 3: Summary of the DETOUR System Biocompatibility Testing

Test Performed	Test Description	Stent Graft	Delivery System	Crossing Device	Results
Cytotoxicity	ISO MEM Elution Using L-929 Mouse Fibroblast Cells	X	X	X	Non-toxic
Sensitization	ISO Guinea Pig Maximization Sensitization Test	X	X	X	Non-sensitizing
Irritation	ISO Intracutaneous Study in Rabbits	X	X	X	Non-irritating
Pyrogenicity	ISO Materials Mediated Rabbit Pyrogen	X	X	X	Non-pyrogenic
Acute Systemic Toxicity	ISO Acute Systemic Toxicity Study in Mice	X[a]	X	X	Non-toxic
Hemocompatibility	ASTM Hemolysis Assay (Direct and Indirect)	X	X	X	Non-hemolytic
	Complement Activation SC5b-9 Assay	X[b]	X[b]	X[b]	Not a complement activator
	In Vivo Thrombogenicity	X[b]			Non-thrombogenic
Genotoxicity	Chemical characterization testing and a toxicological risk assessment	X[a]			Non-mutagenic, non-genotoxic
Subacute / Sub-chronic Toxicity	Chemical characterization testing and a toxicological risk assessment	X[a]			Non-toxic
Chronic Toxicity	Chemical characterization testing and a	X[a]			Non-toxic

Test Performed	Test Description	Stent Graft	Delivery System	Crossing Device	Results
	toxicological risk assessment				
Carcinogenicity	Chemical characterization testing and a toxicological risk assessment	X[a]			Non-carcinogenic

[a] *Evaluated as part of the chemical characterization / toxicological risk assessment*
[b] *Evaluated as part of the GLP chronic animal studies*

The data demonstrated that the medical device materials and processing agents used in the manufacture of the DETOUR System have an acceptable biological safety profile.

B. Animal Studies

Following completion of developmental animal testing, the DETOUR System was subjected to preclinical *in-vivo* evaluations compliant with the requirements of 21 CFR Part 58 – *Good Laboratory Practices for Non-Clinical Laboratory Studies*. These studies were conducted in an ovine animal model. Four chronic studies evaluating near final device design were conducted to support initiation of the DETOUR clinical trials. Two additional definitive ovine studies evaluating the final device were conducted to support approval of the PMA and the results support the safety and performance of the DETOUR System as summarized in **Table 4**.

Table 4: DETOUR System Animal Studies

Study Name	Study Design	Findings
GLP Study of the Performance, Chronic Safety, and Thrombogenicity of the PQ Bypass TORUS Stent Graft using the DETOUR Procedure in an Ovine Model (180 Days)	Ovine (n=8) at 191±1 days On day 90, two of the eight sheep were randomly chosen to be anesthetized and subjected to an interim angiogram procedure to evaluate the target arteries and distal vasculature. The *In-Vivo* Thrombogenicity biocompatibility endpoint was also evaluated.	All study objectives were met in their entirety with no complications at any phase. The test devices passed all evaluation determinants and acceptance criteria. There was no thrombus present on the ENDOCROSS Device or TORUS Stent Graft Delivery System during deployment, and all scores were recorded as "0".
A GLP Study of the Performance, Efficacy, Chronic Safety and Thrombogenicity Evaluation of the PQ Bypass TORUS Stent Graft in the Peripheral Arteries of an Ovine Animal Model at 180 days with an Interim Angiographic	Ovine (n=6) at 180±7 days At the 90-day time point, two study sheep were arbitrarily chosen and subjected to a fluoroscopic evaluation to assess the patency, thrombus, flow or overt pathology within and around the test device.	All study objectives were met in their entirety with no problems encountered at any phase. The test device passed all evaluation determinants and acceptance criteria. None of the study sheep showed signs of thrombus, occlusion, stenosis, or other adverse signs.

Study Name	Study Design	Findings
Evaluation of a Sub-Cohort of Animals and Clinical Pathology at 90 days	The Implantation biocompatibility endpoint was also evaluated.	

C. Cadaver Study

A cadaver evaluation was conducted to confirm the usability of commercially available vascular snares with the DETOUR System during use in the procedure using the DETOUR System. The study considered the following design attributes to compare the usability and performance of snares:

- Venous Access Location
- Snare Outer Diameter
- Device Working Length
- Fluoroscopy Visibility
- Functional Guidewire Capture Area
- Difficulty of Retraction

The cadaver evaluation demonstrated that commercially available vascular snares can meet the usability and performance requirements necessary for the procedure using the DETOUR System.

D. *In Vitro* Bench Testing

In vitro bench testing was performed to support the DETOUR System. Bench testing was performed per Endologix's test protocols, which incorporated applicable international standards and FDA Guidance *Non-Clinical Engineering Tests and Recommended Labeling for Intravascular Stents and Associated Delivery Systems – Guidance for Industry and FDA Staff* (April 2010), as applicable.

Testing was conducted on all device configurations, a subset of device configurations, or worst-case for each test, as appropriate, to represent the entire DETOUR System ranges available. *In vitro* bench testing is summarized in **Table 5**, **Table 6,** and **Table 7** according to testing of the TORUS Stent Graft, TORUS Stent Graft Delivery System, and ENDOCROSS Device.

Table 5: TORUS Stent Graft Testing

Test	Test Purpose	Acceptance Criteria	Results
Dimensional verification	To verify dimensional specifications are met at t=0 and t=12 months accelerated aging.	Test samples must meet design specifications of the device.	PASS
Finite Element Analysis (FEA)	To evaluate the finite element analysis (FEA) results to the self-expanding Torus Stent Graft under simulated *in vivo* pulsatile	FEA is used to determine the worst-case stent graft sizing for durability fatigue testing. Therefore, there is no pre-	Worst case sizes for accelerated durability testing were identified

Test	Test Purpose	Acceptance Criteria	Results
	and multi-mode physiological loading conditions.	defined acceptance criteria for FEA for bending fatigue.	
Accelerated Durability Testing	To evaluate the integrity of the TORUS Stent Graft in a silicone vessel model exposed to biomechanical loading conditions of pulsatile and axial / bending / torsional and crush fatigue for a minimum of 10 years post-implantation.	To stent must maintain structural integrity over a 10-year equivalent of pulsatile and multi-mode bending cycles in intravascular configurations.	PASS
Radial Resistive Force / Chronic Outward Force: TORUS Stent Graft COF/RRF	To assess chronic outward force / radial resistive force at time points t=0 and t=12 months, respectively.	Radial Resistive Force (RRF) ≥0.43 N/mm at 10% compression. Chronic Outward Force (COF) ≥0.14 N/mm and ≤0.60 N/mm at 10% compression.	PASS
TORUS Stent Graft Migration Resistance	To assess intravascular migration resistance at t=0 and t=12 months.	Migration resistance in intravascular placement >1.6N.	PASS
Simulated Use	To verify that the simulated use specifications are met at t=0 and t=12 months accelerated aging for the TORUS Stent Graft System.	The Stent Graft must successfully demonstrate the following functionality: • Shaft flushing • Guidewire compatibility • Catheter flexibility & trackability • Pushability: ≤20N • Outer shaft travel length: 100mm stent: ≥115mm; 200mm stent: ≥220mm • Deployment reliability and accuracy: tracks to location easily and deploys within ±3mm of target • Deployment force: ≤80N	PASS
Stent Integrity	Evaluated following Simulated Use testing. To verify the endoprosthesis has no clinically significant defects or flaws after deployment.	No failures visible under microscope for failures and stent graft portions conform to the mock artery wall. No anomalies (e.g., kinks, twists, component separation, nonuniform expansions, prosthesis damage).	PASS
Permeability: Porosity; Stent	To assess porosity of Torus Stent Grafts at t=0 and t=12 months; to evaluate the WEP of the Torus	Porosity: 5 microns ≤ internodal distance (IND) ≤ 30 microns.	Porosity testing inconclusive. As per ISO 25539-

Test	Test Purpose	Acceptance Criteria	Results
Graft Water Entry Pressure (WEP)	Stent Graft at t=0 and t=12 months.		1:2017 guidance, refer to WEP.
		Water Entry Pressure (WEP): 3 PSI, 155mmHg without gross continuous leaks, streams, or jets of fluid within the body of the stent graft.	PASS
Stent Graft De-Coupling	To evaluate stent graft decoupling force of two overlapped Torus Stent Grafts at time point t=0 and t=12 months.	Decoupling pull force ≥0.8N ≥6cm overlap).	PASS
Local Compression Testing	To evaluate local compression at t=0 and t=12 months.	≥1.4N when compressed by 75% to 25% of nominal OD.	PASS
Flex/Kink Testing	To evaluate flex/kink resistance of the Torus Stent Graft at t=0 and t=12 months.	The stent must not kink at a 15mm bend radius without kinking (50% lumen loss).	PASS
Burst Testing	To evaluate burst testing of the Torus Stent Graft at t=0 and t=12 months.	Device can withstand ≥42kPa (6psi) of hydrostatic pressure delivered at a continuous rate of 10kPa/second.	PASS
Tensile Testing	To evaluate the longitudinal tensile strength of the Torus Stent Graft at t=0 and t=12 months.	Tensile strength must be ≥15N.	PASS
Corrosion Testing for Bare Stent Frame	To evaluate the crevice and pitting corrosion resistance of the bare Torus stent frame, i.e., with no ePTFE membrane.	The stent must have a minimum breakdown potential above 400 mV.	The endoprosthesis exhibits acceptable corrosion resistance based on testing per ASTM F2129-19a.
MRI Compatibility for Overlapping Torus Stent Grafts	To assess the safety and compatibility of the stent in the MRI environment.	The stent shall be MR conditional to 1.5 and 3 Tesla.	The stent does not pose additional risk to patients and may be labeled MR Conditional according to ASTM 2503.
Material Composition	Characterize the stent material composition to ensure it is acceptable for the intended use.	Chemical composition is within specification and complies with ASTM F2063-12.	The stent material conforms to implant material standards.
Mechanical Properties	Characterization testing performed to determine tensile and fatigue properties as inputs to support stress/strain and fatigue analysis.		

Test	Test Purpose	Acceptance Criteria	Results
Austenite Finish Temperature (A_f) Testing	To evaluate the A_f transformation temperature of the stent per ASTM F2082/F2082M.	A_f temperatures of 9 ± 5°C.	PASS

Table 6: TORUS Stent Graft Delivery System Testing

Test	Test Purpose	Acceptance Criteria	Results
Dimensional Verification	To verify dimensional specifications are met at t=0 and t=12 months accelerated aging.	Test samples must meet design specifications of the device.	PASS
Simulated Use	See summary under TORUS Stent Graft Testing at t=0 and t=12 months accelerated aging.	See summary under TORUS Stent Graft Testing.	PASS
Bond/Joint Strength	To evaluate the strength of delivery system bonds at t=0 and t=12 months accelerated aging.	The delivery system bonds must maintain integrity above the specified load levels during stent deployment and delivery system retraction.	PASS
Kink Resistance	To verify that the Stent Graft Delivery System is resistant to kinking at t=0 and t=12 months accelerated aging.	Catheter will not kink when navigating a simulated anatomy with a radius of curvature 26.30mm.	PASS
Atraumatic Tip	To ensure that the force exerted by the Stent Graft Delivery System tip minimizes trauma to vessels during use at t=0 and t=12 months accelerated aging.	Force by the distal tip of the Delivery System is ≤20N.	PASS
Torque Strength	To assess the torque strength of the Stent Graft Delivery System at t=0 and t=12 months accelerated aging.	The stent graft delivery system must withstand handle rotations up to and including 360° clockwise and counterclockwise.	PASS

Table 7: ENDOCROSS Device Testing

Test	Test Purpose	Acceptance Criteria	Results
Dimensional Verification	To verify dimensional specifications are met at t=0 and t=12 months accelerated aging.	Test samples must meet design specifications of the device.	PASS
Simulated Use Testing	To verify that the ENDOCROSS Device simulated use specifications are met at t=0 and t=12 months accelerated aging.	The device must successfully demonstrate the following functionality: • Guidewire Rapid Exchange compatibility • Guidewire, needle compatibility	PASS

Test	Test Purpose	Acceptance Criteria	Results
		• Needle & stabilizer deployment control and multiple deployment and retractions • Catheter flushing • Catheter trackability • Catheter pushability: ≤20N • Catheter retraction force: ≤20N • Needle guidewire retraction force: ≤3N	
Bond/Joint Strength	To verify that the ENDOCROSS Device bond strength specifications are met at t=0 and t=12 months accelerated aging.	The delivery system bonds must maintain integrity above the specified load levels during use.	PASS
Kink Resistance	To verify that the ENDOCROSS Device is resistant to kinking at t=0 and t=12 months accelerated aging.	Catheter will not kink when navigating simulated anatomy with a radius of curvature of 26.30mm (1.04 inches) at the inner surface.	PASS
Atraumatic Tip	To determine, at t=0 and t=12 months accelerated aging: (1) tensile force that will separate the distal tip on the ENDOCROSS Device, and (2) pressure exerted by the ENDOCROSS Device stabilizer to a simulated artery.	Atraumatic tip: ≤12N Atraumatic stabilizer: ≤4psi in 4mm simulated artery	PASS
Needle Function	To verify, at t=0 and t=12 months accelerated aging: (1) distal end of the ENDOCROSS Device is non-coring, and (2) ability of the needle to puncture both arterial and venous walls in a single stroke during use.	Non-coring needle: No visible simulated tissue present after test. Needle penetration: Needle penetrates through two 0.006" thick sheets of polyethylene with three needle firings.	PASS
Torque Response and Torque Strength	To assess the torque ability of the ENDOCROSS Device distal tip and the number of rotations until failure of the ENDOCROSS Device at t=0 and t=12 months accelerated aging.	Torque response: Amount of torque transmitted ≤300° Torque strength: The catheter must withstand handle rotations up to and including 360° clockwise and counterclockwise.	PASS

E. Sterilization

The DETOUR System (TORUS Stent Graft System and ENDOCROSS Device) is single-use and terminally sterilized using Ethylene Oxide (EO). The sterilization process is validated to demonstrate a sterility assurance level (SAP) of 10^{-6} in accordance with ISO 11135:2014: *Sterilization of health care products – Ethylene oxide: Requirements for development, validation and routine control of a sterilization process for medical devices*.

F. Packaging and Shelf Life

Packaging tests of the DETOUR System were conducted to verify that the integrity, as well as safety and performance, were not compromised due to the effects of storage and packaging stress. Baseline and aged packaging testing included a visual assessment, gross (bubble) leak testing, seal tensile strength, simulated shipping and distribution testing of the TORUS Stent Graft System and ENDOCROSS packaging. All tests passed requirements. A shelf life of one (1) year has been established for the DETOUR System based on product and package shelf-life testing.

X. SUMMARY OF PRIMARY CLINICAL STUDY

The applicant performed a clinical study (DETOUR2) to establish a reasonable assurance of safety and effectiveness of the procedure with the DETOUR System for percutaneous revascularization in patients with symptomatic femoropopliteal lesions from 200mm to 460mm in length in the US, Latvia, and Germany under IDE G170083. 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 in the DETOUR2 study between December 13, 2017, and October 5, 2020. The database for the PMA reflected data collected through November 15, 2022, and included 220 patients. There were 36 investigational sites.

The study was a prospective, multi-center, single-arm, international, non-randomized premarket clinical study to evaluate the safety and effectiveness of the DETOUR System for the percutaneous treatment of patients with symptomatic femoropopliteal occlusive disease, as assessed in comparison to the prespecified safety and effectiveness performance goals (PGs).

The primary safety endpoint was freedom from major adverse events (MAEs) through 30 days post-procedure. Major Adverse Events include death, clinically driven target lesion revascularization (CD-TLR), amputation of the treated limb, occlusive-symptomatic deep vein thrombosis (DVT), pulmonary embolism (PE), or procedure-related bleeding requiring any transfusion of packed red blood cells or surgery. A performance goal for freedom from 30-day MAE of 84.0% was established for this endpoint. The safety performance goal was based on an aggregate of published trial data as described by VIVA Physicians Inc. (VPI) and adjusted to reflect the greater risk associated with the DETOUR2 study population. The study

device was considered to have achieved the safety objective if the lower limit of the one-sided lower 97.5% confidence limit based on the exact method is greater than 84%.

The primary effectiveness endpoint was patency at 12 months post procedure. Patency is defined as the absence of CD-TLR and absence of recurrent target lesion diameter stenosis >50% by imaging (e.g., duplex ultrasound peak systolic velocity ratio peak systolic velocity ratio [PSVR] of >2.5 within the stent or immediately 1cm above or below the treated segment). If both duplex ultrasound and angiography were available, angiography took precedence. The primary effectiveness endpoint of 12-month patency was evaluated by comparing the proportion of successful subjects to a literature-derived performance goal of 60.4%.

The final study sample size was based on the number required to test the primary effectiveness endpoint. To account for a 10% attrition rate, it was calculated that 202 subjects should be enrolled such that 181 subjects were expected to provide evaluable data for the 12-month patency endpoint.

An independent Clinical Events Committee (CEC) was used to review and adjudicate primary and secondary safety endpoints (defined in the study protocol), including major adverse events. A Data Safety Monitoring Board (DSMB) consisting of non-Investigator experts, reviewed safety data and established stopping rules for early termination of the trial. All angiograms, duplex ultrasound studies and x-rays obtained during this study per study requirements were submitted to the central Imaging Core Lab for analysis. The Core Lab assessed x-ray imaging for stent fracture at the applicable study time points. An independent Medical Monitor (MM) reviewed each adverse event to determine endpoints in accordance with guidelines provided by the CEC Charter.

1. Clinical Inclusion and Exclusion Criteria

Enrollment in the DETOUR2 Study was limited to patients who met the following inclusion criteria:

General Inclusion Criteria

- Age > 18 and ≤ 90 years.
- Willing and above to provide informed consent.
- Subject is willing to undergo all follow-up assessments according to the specified schedule over 36 months.

Clinical Inclusion Criteria

- Chronic, symptomatic lower limb ischemia defined as Rutherford Clinical Categories 3, 4, or 5.
- Venous Clinical Severity Score <3.
- Subject is a suitable candidate for angiography and endovascular intervention and, if required, is eligible for standard surgical repair.

Angiographic Inclusion Criteria

- Symptomatic femoropopliteal chronic total occlusions ≥20 cm (TASC D) that can include de novo, restenotic, or in-stent restenotic lesions; or
- Symptomatic femoropopliteal lesions ≥24 cm (total lesion length) that can include a chronic total occlusion or a ≥70% lesion that includes de novo, restenotic or in-stent restenosis (complex TASC C), by investigator visual assessment.
- Reference vessel diameter ≥4.5 and ≤6.7 mm, by investigator visual assessment
- Subject has a patent popliteal artery (<50% stenosis) distal to the landing zone.
- Able to successfully access the SFA origin for entry of the crossing device.
- At least one patent infrapopliteal vessel (<50% stenosis) with run-off to the ankle or foot.
- A significant stenosis (≥50%) or occlusion of an ipsilateral, inflow artery (e.g., aortoiliac, common femoral) must be successfully treated (use of investigational treatment prohibited) prior to treatment of the target lesion. Successful treatment is defined as no complications and less than 30% residual stenosis following intervention.

Patients were not permitted to enroll in the DETOUR2 study if they met any of the following exclusion criteria:

General Exclusion Criteria

- Participating in another investigational study.
- Anticipated life expectancy less than 1 year or medical comorbid condition(s) that could limit the subject's ability to comply with the requirements of the trial.
- Subject has other medical, social or psychological problems that, in the opinion of the investigator, preclude them from receiving this treatment, and the procedures and evaluations pre- and post-treatment.

Clinical Exclusion Criteria

- History of deep vein thrombosis on either limb.
- Thrombophlebitis, within the previous 30 days.
- Subject has a known coagulopathy or has bleeding diatheses, thrombocytopenia with platelet count less than 100,000/microliter or INR >1.8.
- Planned amputation of the target limb, including minor amputations.
- Prior distal amputation (above the trans metatarsal) of the target limb.
- Known or suspected active infection at the time of the procedure (e.g., WIfI foot infection grade 3: Severe infection. Local infection systemic inflammatory response syndrome [SIRS]).
- Rutherford Clinical Category 0, 1, 2 or 6.
- Has acute or chronic renal disease with GRF ≤30 ml/min per 1.73 m^2 and/or elevated serum creatinine >2.5 mg/dL (220 µmol/L) or on dialysis.
- Known hypersensitivity/allergy to the investigational devices and/or required pharmacotherapy that cannot be safely managed.
- Morbid obesity that does not allow for safe vascular access or imaging.

- Requires coronary or peripheral procedure within 30 days prior to or planned within 30 days post treatment of the target lesion.
- Has a known history of intracranial bleeding or aneurysm, myocardial infarction or stroke within the last 3 months.
- Subject is pregnant or breast-feeding.

Angiographic Exclusion Criteria

- Stent within 3cm of SFA ostium.
- Previous bypass surgery on the target limb.
- Subject has significant disease or obstruction (≥50%) of the inflow tract that has not been successfully treated at the time of the index procedure (success measured as ≤30% residual stenosis, without complication).
- Presence of aneurysm or acute thrombus in the target limb.
- Thrombolysis of the target vessel within 72 hours prior to the index procedure, where complete resolution of the thrombus was not achieved.

2. Follow-up Schedule

All patients were scheduled to return for follow-up examinations at 1 month (±7 days), 6 months (±30 days), 12 months (±30 days), 24 months (±60 days), and 36 months (±60 days) post-procedure or when a subject withdrew prematurely from the study. The schedule of evaluations to be completed at each study interval is presented in **Table 8**.

Table 8: Evaluations to be Completed at Each Study Interval

Activity	Pre-procedural Baseline Screening	Procedure	Discharge	Follow-Up Visits (M)				
				1	6	12	24	36
Review of Inclusion / Exclusion Criteria	X	X						
Medical History / Demographics	X							
Brief Physical Exam / Health Status	X		X	X	X	X	X	X
Routine Laboratory Tests (CBC and Chem-7)	X							
Serum Creatinine to Calculate eGFR	X							
Ankle-Brachial Index (or Toe-Brachial Index[1])	X			X	X	X	X	X
Rutherford Assessment	X			X	X	X	X	X

Activity	Pre-procedural Baseline Screening	Procedure	Discharge	Follow-Up Visits (M)				
				1	6	12	24	36
Venous Clinical Severity Score and Villalta Scale	X			X	X	X	X	X
Final Eligibility Angiograph / Venogram or Venous Ultrasound[2]		X						
Venous Ultrasound[3] and Venous Observation Scale				X	X	X	X	X
Arterial Ultrasound[3]				X	X	X	X	X
Stent Graft X-Ray						X		
Adverse Event Assessment		X	X	X	X	X	X	X
Dual Antiplatelet Therapy[4]	X	X	X	X	X	X	X	X
VascuQOL	X			X		X		
EQ-5D-5L QOL	X			X		X		
SF-12	X			X		X		
6 Minute Walk Test[5]	X			X		X		

[1] Perform Toe Brachial Index (TBI) only if unable to reliably assess ABI reading. Tests are performed in resting state.
[2] Angiography performed throughout the index procedure. Angiography required to be submitted to the angiographic core lab for all target limb revascularization procedures.
[3] Duplex Ultrasound is to be completed at each follow-up visit.
[4] Effective anticoagulation therapy should be maintained throughout the procedure (minimum ACT >250 seconds is recommended). Dual anti-platelet or anti-coagulation therapy is recommended for at least three years.
[5] The 6-Minute Walk Test is not routinely performed at all clinical sites; therefore, select sites shall complete a 6MWT on select subjects as agreed upon. This will therefore result in a sub-group of clinical sites and subjects and not be study wide.

3. Clinical Endpoints

The primary safety endpoint was freedom from major adverse events (MAEs) through 30 days post-procedure. The performance goal of freedom from primary safety event is 84.0%, which was set at 4% below the aggregate of published trial data as described by VIVA Physicians Inc. (VPI). The primary safety hypothesis was tested by calculating the lower one-sided 97.5% confidence limit, using the Exact method, for the rate of freedom from MAEs. The primary safety endpoint was evaluated on a per subject basis and was calculated as the percent of all Intent to Treat (ITT) subjects that are free from all elements of the primary safety endpoint composite at 30 days.

The primary effectiveness endpoint was primary patency at 12 months post procedure. Primary patency is defined as the absence of clinically driven target lesion revascularization (CD-TLR) and absence of recurrent target lesion diameter stenosis >50% by imaging (e.g., duplex ultrasound peak systolic velocity ratio peak systolic velocity ratio [PSVR] of >2.5 or as measured by invasive angiography) within the stent or immediately 1 cm above or below the treated segment.

The primary effectiveness endpoint was evaluated against a literature-derived performance goal (PG) of 60.4%, which was determined as the weighted mean of historical studies of endovascular treatment of similar lesions. The primary effectiveness hypothesis was tested by calculating the one-sided lower 97.5% confidence limit, using the Exact method. The primary effectiveness endpoint was evaluated on patients who received the device and with evaluable images as defined in Section X.B. Accountability of PMA Cohort.

Secondary Endpoints

The following secondary safety endpoints were evaluated:

- Major Adverse Events (MAE) at 6, 12, 24 and 36 months.
- Major Adverse Limb Event (MALE) defined as above-ankle amputation or major reintervention including placement of a new bypass graft, interposition graft, thrombectomy, or thrombolysis.
- Major bleeding is defined as any bleeding event requiring transfusion of ≥2 units packed red blood cells (PRBC) or surgical repair through 30 days.
- Symptomatic Deep Vein Thrombosis (DVT) on ipsilateral limb at 30 days and 6, 12, 24 and 36 months.
- Pulmonary embolism at 30 days and 6, 12, 24 and 36 months.
- Perioperative myocardial infarctions through 30 days.
- Hematoma ≥8cm related to the device or procedure through 30 days.
- The combined rate of death, target lesion revascularization (TLR), index limb amputation, and an increase in Rutherford Clinical Category by 2 classes (comparing pre- to post-procedural assessments) at 30 days and 6, 12, 24 and 36 months.
- Stent graft separation and migration identified via ultrasound imaging at 30 days and 6, 12, 24 and 36 months.
- Stent graft separation and migration identified via x-ray at 12 months.
- Stent graft fracture identified via x-ray at 12 months.

The following secondary effectiveness endpoints were evaluated:

- Technical Success defined as successful delivery of the investigational devices to the identified area and removal of delivery system.
- Procedural Success defined as successful delivery of the investigational devices to the identified area and removal of delivery system in the absence of in-hospital MAEs.

- Clinical Success defined as limb ischemia improvement as assessed by Rutherford Clinical Category (improvement in scale by ≥1) at 30 days and 6, 12, 24 and 36 months.
- Limb ischemia by Rutherford Clinical Category through follow-up at 30 days and 6, 12, 24 and 36 months.
- Primary Patency at 30 days and 6, 24 and 36 months.
- Primary assisted patency defined as revascularization of nonocclusive (<99%) stenosis within the stent graft or immediately above or below the treated arterial segment with less than 50% residual stenosis at 30 days and 6, 12, 24 and 36 months.
- Secondary patency defined as revascularization of occlusion (100%) within the stent graft or immediately above or below the treated arterial segment with less than 50% residual stenosis at 30 days and 6, 12, 24 and 36 months.
- Target Vessel Revascularization defined as any repeat percutaneous intervention or surgical bypass of any segment of the target vessel at 30 days and 6, 12, 24 and 36 months.
- Ankle-Brachial Index (ABI) or Toe Brachial Index (TBI) of both the index limb and contralateral limb at 30 days and 6, 12, 24 and 36 months.
- Number of major index limb amputations at 30 days and 6, 12, 24 and 36 months.
- Major procedure-related infections within 30 days.
- Length of post-procedure hospital stay.
- Length of ICU stay.
- Hospital re-admissions through 30 days.
- Change from baseline in VascuQol QOL Score at 30 days and 12 months.
- Change from baseline in EQ-5D-5L QOL Score at 30 days and 12 months.
- Change from baseline in Duplex Venous Observation Scale at 30 days and 6, 12, 24 and 36 months.
- Change from baseline in Villalta and Venous Clinical Severity (VCSS) Scales at 30 days and 6, 12, 24 and 36 months.
- SF-12 Score at baseline, 30 days and 12 months.

Subgroup Analyses

The following subgroups were analyzed for the primary endpoints: Female gender, diabetics, and US cohorts.

B. Accountability of PMA Cohort

At the time of database lock, 220 patients enrolled in the DETOUR2 study at 36 sites. 85.5% (188) patients are available for analysis for the 12-month post-operative visit. Overall, 220 subjects were treated with the ENDOCROSS Device.

The analyzed patient cohorts are defined as:

Roll-ins: The first two subjects at each U.S. site may be considered roll-in subjects. Roll-in subjects were pre-identified. Not all sites enrolled roll-in subjects.

Intention to Treat (ITT): All subjects who received the intervention and were enrolled in the IDE Study (excluding roll-ins). The ITT Cohort was the primary analysis set to determine if the primary safety endpoint was met in the study.

Modified ITT (MITT): Only those subjects/lesions where a DETOUR System: TORUS Stent Graft was implanted. The MITT Cohort is a subset of the ITT Cohort. The MITT Cohort is the primary analysis set to determine if the primary effectiveness endpoint was met in the study.

Per Protocol (PP): Subset of the MITT group which excludes all subjects with major protocol deviations (e.g., violations of eligibility criteria) and missing the data required to evaluate the primary effectiveness endpoint.

Of the 220 subjects who received the ENDOCROSS Device, 18 were considered roll-in subjects and remaining 202 (91.8%) are considered part of the ITT Cohort. Two subjects from the ITT group did not receive the TORUS Stent Graft, thus 200 patients were part of the MITT Cohort. Of the MITT Cohort, 197 (89.5%) were considered part of the Per Protocol Cohort.

Figure 5 depicts the accountability of subjects at the study follow-up time points. Of the 220 subjects enrolled, 83.6% (184) patients are available for analysis for the 12-month post-operative visit. Eighteen (18) subjects in the ITT group exited before the 12-month window: 2 enrolled but did not receive the ENDOCROSS device, 7 subject withdrawals, 2 physician withdrawal, 5 deaths, and 2 lost-to-follow-up.

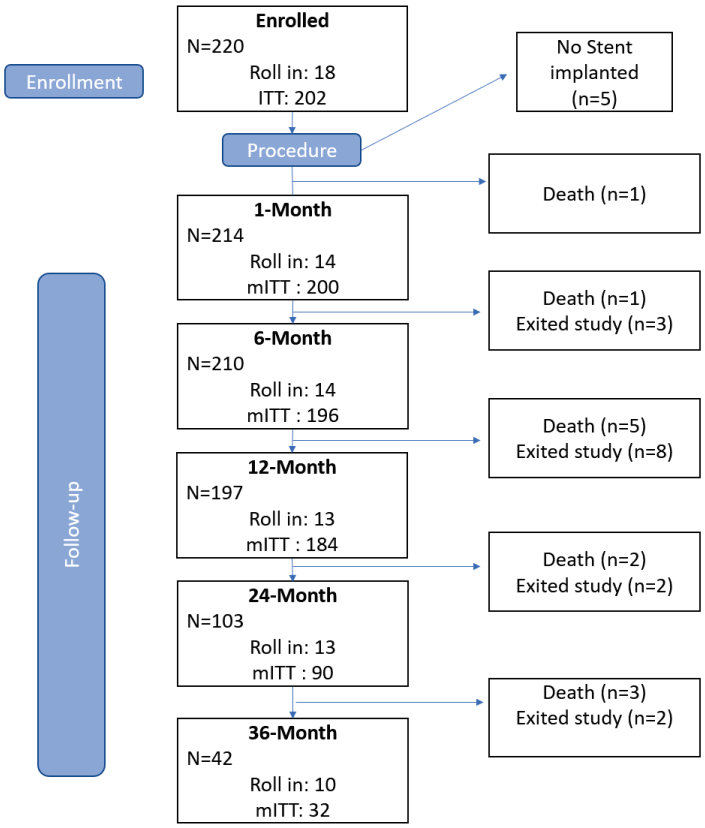

Figure 5: Subject Disposition

C. Study Population Demographics and Baseline Parameters

Specific demographics and baseline characteristics for the DETOUR2 Study ITT population are presented in **Table 9**. Medical history and health status are provided in **Table 10**. Sub-group analysis of the ITT population is provided in Section D Safety and Effectiveness Results.

The mean age was 68.9 ±9.4 years and 26.2% were female. 86.6% of the patients were white. Comorbidities included coronary artery disease (87.6%), hypertension (87.6%), diabetes (34.7%), prior history of smoking (91.1%), and renal insufficiency (10.9%). The mean ABI was 0.61 ±0.22 at baseline. Most patients (77.7%) were Rutherford Clinical Category (RCC) 3. The remainder of the patients (22.3%) were RCC 4 and RCC 5.

Table 9: Baseline Demographics - ITT Population

Variable	All Subjects
Age at Consent (years)	68.9 ± 9.38 (202) 69.0 (47, 88)
Body Mass Index (BMI)	28.74 ± 5.028 (202) 28.50 (18.3, 45.0)

Variable	All Subjects
Sex	--
Female	26.2% (53/202)
Male	73.8% (149/202)
Race[1]	--
American Indian or Alaska Native	0.5% (1/202)
Asian	0.0% (0/202)
Black or African American	8.9% (18/202)
Native Hawaiian or Other Pacific Islander	0.0% (0/202)
White	86.6% (175/202)
Other	4.5% (9/202)
Ethnicity	--
Hispanic or Latino	4.6% (9/196)
Not Hispanic or Latino	79.6% (156/196)
Not Reported	15.8% (31/196)

Categorial variables presented as % (n/N) and continuous variables presented as mean ± SD (N) median (min, max) where N is the number of subjects with available data.
[1]One subject identified under two (2) categories (White, American Indian or Alaska Native).

Table 10: Medical History and Health Status – ITT Population

Variable	All Subjects
Renal Insufficiency (with or without intervention)	10.9% (22/202)
History of Smoking	--
Current/Previous	91.1% (184/202)
Never	8.9% (18/202)
History of Peripheral Venous Disease (DVT, Thrombophlebitis, etc.)	0.0% (0/202)
Peripheral Arterial Disease	98.0% (198/202)
Previous Peripheral Intervention	60.5% (121/200)
Previous Peripheral Vascular Surgery	16.8% (34/202)
Hypertension	87.6% (177/202)
Diabetes Mellitus	34.7% (70/202)
Type 1	1.4% (1/70)
Type 2	98.6% (69/70)
Hypercholesterolemia	73.2% (145/198)

Variable	All Subjects
Hyperlipidemia	73.3% (140/191)
Coronary Artery Disease	46.0% (92/200)
Congestive Heart Failure	12.4% (25/201)
NYHA I	16.0% (4/25)
NYHA II	48.0% (12/25)
NYHA N.A.	36.0% (9/25)
History of Myocardial Infarction	21.9% (44/201)
History of Cerebrovascular Disease	13.9% (28/201)
Stroke	60.7% (17/28)
TIA	21.4% (6/28)
Other	17.9% (5/28)
Target Limb Ankle-Brachial Index (ABI)	0.61 ± 0.22 (193) 0.60 (0.00, 1.55)
Contralateral Limb Ankle-Brachial Index (ABI)	0.82 ± 0.26 (189) 0.82 (0.00, 1.63)
Target Limb Toe-Brachial Index (TBI)	0.45 ± 0.19 (58) 0.43 (0.00, 0.83)
Contralateral Limb Toe-Brachial Index (TBI)	0.59 ± 0.23 (57) 0.60 (0.00, 1.10)
Rutherford Clinical Category	--
Grade 3	77.7% (157/202)
Grade 4	17.8% (36/202)
Grade 5	4.5% (9/202)

Categorical variables presented as % (n/N) and continuous variables presented as mean ± SD (N) median (min, max) where N is the number of subjects with available data.

Table 11 summarizes the baseline lesion characteristics determined by the Core Lab. Target lesions were relatively equally distributed between the right and left limb. Pre-procedure chronic occlusion (CTO; 100% stenosis) was observed in 96.0% (194/202) of subjects and diffuse stenosis (>70% stenosis) was observed in 97.0% (196/202) of subjects. The mean lesion length was 327.14 ± 61.38mm. The mean CTO length was 217.31 ± 85.98mm. The calcification grade for lesions was predominantly severe (70.4%, 126/179) followed by none/mild (29.1%, 52/179) and then moderate (0.6%, 1/179).

Two vessel run-off to the foot was observed in 69.0% (129/187) of subjects. There were no subjects who had zero run-off vessels to the foot. The popliteal artery was involved in approximately 10% of lesions, and approximately 44% of subjects had below-the-knee arterial disease as well.

Table 11: Core Lab Baseline Lesion Characteristics - ITT Population

Variable	All Subjects
Total Occlusion (100% stenosis)	96.0% (194/202)
Diffuse Stenosis (>70% stenosis)	97.0% (196/202)
In-Stent Restenosis	17.3% (35/202)
Lesion Length (Normal to Normal, mm)	327.14 ± 61.38 (196) 328.15 (194.6, 520.3)
Calcified Length (mm)	64.12 ± 77.50 (178) 41.10 (0.0, 415.7)
CTO Length (mm)	217.31 ± 85.98 (191) 232.50 (0.0, 436.1)
Calcification	--
None/Mild	29.1% (52/179)
Moderate	0.6% (1/179)
Severe	70.4% (126/179)

Categorical variables presented as % (n/N) and continuous variables presented as mean ± SD (N) median (min, max) where N is the number of subjects with available data.

Of the 202 ITT subjects, the device was implanted in 200. Two (2) subjects did not receive the device: one (1) case was aborted because there was a complication with a percutaneous transluminal angioplasty (PTA) balloon which extended the procedure time, and one (1) case was aborted because venous access was difficult.

Table 12 summarizes site reported procedure characteristics. The majority of subjects were treated under conscious sedation (40.6%; 82/202) or local anesthesia (28.2%; 57/202). Mean procedure time was 181.4 ± 90.55 minutes, with a mean fluoroscopy time of 46.4 ± 19.51 minutes. An average of 208.1 ml ± 111.74 of contrast was used per subject. Estimated blood loss was 50 ± 57.50 ml per subject.

Table 12: Site Reported Procedure Characteristics - ITT

Variable	All Subjects
Type of Anesthesia Used	--
General	12.4% (25/202)
Local	28.2% (57/202)
Epidural/Spinal	5.9% (12/202)
Conscious Sedation	40.6% (82/202)
Other	12.9% (26/202)
Estimated Blood Loss (ml)	50.0 ± 57.50 (201) 30.0 (0, 400)
Contrast Volume Used (ml)	208.1 ± 111.74 (199) 180.0 (50, 900)

Variable	All Subjects
Fluoroscopy Time (min)	46.4 ± 19.51 (199) 42.0 (12, 122)
Total Procedure Time (min)	181.4 ± 90.55 (202) 163.0 (55, 495)

Categorical variables presented as % (n/N) and continuous variables presented as mean ± SD (N) median (min, max) where N is the number of subjects with available data.

Core laboratory reported post-procedure angiographic data are presented in **Table 13**.

Table 13: Post-Procedure Core Lab Angiography Data

Post-Procedure Characteristics	All Subjects
Distance of Proximal TORUS Edge from Superficial Femoral Artery Ostium (mm)	5.91 ± 5.672 (183) 4.40 (0.0, 50.8)
Distance from Distal TORUS Edge to Tibial Plateau (mm)	42.55 ± 36.22 (183) 28.00 (2.4, 150.5)
Proximal Intra-Arterial TORUS Length	48.10 ± 17.68 (187) 45.90 (13.2, 125.6)
Distal Intra-Arterial TORUS Length	59.44 ± 20.82 (187) 54.40 (19.2, 129.4)
Overlap Lengths (mm)	--
Proximal (or only)	72.00 ± 20.54 (169) 69.00 (28.5, 139.1)
Middle	43.60 ± 23.11 (3) 35.80 (25.4, 69.6)
Distal	66.14 ± 16.54 (134) 63.15 (28.1, 179.9)
Run-Off Vessels to the Foot	--
0	0.0% (0/183)
1	15.3% (28/183)
2	67.2% (123/183)
3	17.5% (32/183)

Categorical variables presented as % (n/N) and continuous variables presented as mean ± SD (N) median (min, max) where N is the number of subjects with available data.

Technical success in the MITT population, defined as successful delivery of the investigational devices to the identified area and removal of delivery system was 100%, in the 200 subjects. Procedural success in the MITT population, defined as successful delivery of the investigational device to the identified area and removal of the delivery system in the absence of in-hospital MAEs, was 98.5% (197/200). Three (3) patients had MAEs prior to

discharge: Two (2) subjects were reported to have major bleeding, and one (1) subject was reported to have had a symptomatic DVT.

D. Safety and Effectiveness Results

1. Safety Results

The primary safety endpoint was freedom from a composite of Major Adverse Events (MAE) at 30 days (**Table 14**) as adjudicated by the CEC. MAEs were defined as any of the following: all-cause mortality, CD-TLR, amputation of the treated limb, occlusive-symptomatic deep vein thrombosis, pulmonary embolism, or procedure-related bleeding. There were 15 total 30-day MAEs in 14 subjects: 3 CD-TLR, 5 DVT and 7 major bleeding events.

There were 199 subjects of the 202 subjects in the ITT group evaluated for the primary safety endpoint at 30 days. Freedom from MAE at 30 days was 93.0% (185/199), with a lower exact one-sided 97.5% confidence interval of 88.5% compared to the PG 84%. Thus, the primary safety endpoint was met. The composite primary safety endpoint is summarized in **Table 14**. There were 199 subjects of the 202 subjects in the ITT group evaluated for the primary safety endpoint at 30 days. The 30-day MAE rate for the roll-in cohort (n=18) was comparable to the pivotal [ITT] cohort (5.6% in roll-in versus 7.0% in pivotal ITT).

Major adverse events are reported in **Table 15**. Follow-up is on-going through 36 months.

Table 14: Freedom from Major Adverse Event (MAE) at 30 Days - ITT Population

	All Subjects	Lower 97.5% Exact Confidence Limit
Freedom from MAE[1]	93.0% (183/199)[2] 15 total 30-day MAE events in 14 subjects: • 3 CD-TLR • 5 DVT • 7 Major Bleeding Events	88.5% > 84% P

[1] Freedom from a major adverse event (MAE) at 30-days post-procedure defined as any occurrence of the following events: Death, Clinically Driven Target Lesion Revascularization (CD-TLR), Amputation of the Treated Limb, Symptomatic Deep Vein Thrombosis (DVT), Pulmonary Embolism (PE) or procedure-related bleeding requiring any transfusion of packed red blood cells or surgery.
[2] There were 199 subjects of the 202 subjects in the ITT group evaluated for the primary safety endpoint at 30 days.

Table 15: Major Adverse Events Over Time: Kaplan Meier Estimates - ITT Population

Event	30 Days	6 Months	12 Months
MAE	7.0% [3.5%, 10.5%]	13.6% [8.8%, 18.3%]	19.8% [14.2%, 25.4%]

Event	30 Days	6 Months	12 Months
Death Events[1]	0.0% [0.0%, 0.0%]	0.5% [0.0%, 1.5%]	2.6% [0.4%, 4.9%]
CD-TLR	1.5% [0.0%, 3.2%]	6.6% [3.1%, 10.0%]	12.3% [7.7%, 17.0%]
Amputation of Treated Limb	0.0% [0.0%, 0.0%]	1.0% [0.0%, 2.4%]	2.1% [0.1%, 4.1%]
Deep Vein Thrombosis	2.5% [0.3%, 4.7%]	3.5% [1.0%, 6.1%]	4/1% [1.3%, 6.8%]
Pulmonary Embolism	0.0% [0.0%, 0.0%]	0.0% [0.0%, 0.0%]	0.0% [0.0%, 0.0%]
Procedure Related Bleeding	3.5% [1.0%, 6.0%]	3.5% [1.0%, 6.0%]	3.5% [1.0%, 6.0%]

Data presented as % (n/N) [m] where n is the number of subjects experiencing at least 1 event, N is the number of subjects, and m is the total number of events.

[1] There were 11 adverse events that resulted in death: none of these adverse events were related to the device or the procedure. Three (3) deaths were reported for unknown causes.

Serious Adverse Events that Occurred in the PMA Clinical Study:

Overall, 66.3% (134/202) of subjects had a serious adverse event (SAE) within 12 months; almost half were vascular disorders based on the System Organ Category (SOC) classification. Of all SAEs, 24.3% (49/202) were device related SAEs, as adjudicated by the CEC. The most common SOC for device-related SAEs were Vascular Disorders, with 48/202 subjects (23.8%) experiencing at least one SAE in the SOC.

Overall, 17.3% (35/202) procedure related SAEs were adjudicated by the CEC, were observed through 12-months. The most common SOC for procedure-related SAEs was Vascular Disorders, with 21/202 subjects (10.4%) experiencing at least one adverse event in this SOC.

Table 16: Serious Adverse Events – ITT Population

Adjudicated Event	Body System or Organ Class / Preferred Level Term	Through 12 Months % (n/N) [m]
All Serious Adverse Events	Any Event	66.3% (134/202) [355]
	Vascular Disorders	48.5% (98/202) [167]
Serious Device Related Adverse Event	Any Event	24.3% (49/202) [67]
	Vascular Disorders	23.8% (48/202) [59]

Adjudicated Event	Body System or Organ Class / Preferred Level Term	Through 12 Months % (n/N) [m]
Serious Procedure Related Adverse Event	Any Event	17.3% (35/202) [57]
	Vascular Disorders	10.4% (21/202) [26]

Data presented as % (n/N) [m] where n is the number of subjects experiencing at least 1 event, N is the number of subjects, and m is the total number of events.

2. Secondary Safety Endpoints

Secondary safety endpoint Kaplan Meier Estimates were performed on the ITT analysis set (**Table 17**). Major Adverse Limb Events (MALE) were reported at 30 days, 6 months, and 12 months, with a rate of 4.0%, 10.5%, and 15.7%, respectively.

Major Bleeding was reported in eight (8) subjects, with nine (9) events occurring within 30 days of the index procedure. Eight (8) of these events were related to the procedure. Five (5) of these eight (8) procedural related events were due to blood loss anemia, there were two (2) gastrointestinal bleeds and one retroperitoneal hematoma.

Symptomatic DVT occurred in eight (8) subjects through 12 months with no new symptomatic DVT in the subjects followed through 24 months and 36 months. Most DVT (7/8) occurred within 6 months of the index procedure. There has been no Pulmonary Embolism (PE) observed in the ITT Cohort at the time of this report. There was one (1) perioperative Myocardial Infarction (MI) in the ITT population, through 30 days (0.5%; 1/199). There were three (3) MIs through 12 months in the ITT cohort and seven (7) MIs total in patients followed through 36 months.

The percentage of hematoma (≥8 cm) within 30 days of the index procedure that were related to the device or procedure is 0.5% (1/199). At 30-days follow-up, the stent thrombosis Kaplan Meier estimate was 3.5%.

Table 17: Secondary Safety Endpoints Over Time: Kaplan Meier Estimates – ITT Population

Event	30 Days	6 Months	12 Months
Major Adverse Limb Events (MALE)	4.0% [1.3%, 6.7%]	10.5% [6.3%, 14.8%]	15.7% [10.7%, 20.9%]
Major Bleeding	4.0% [1.3%, 6.7%]	6.0% [2.7%, 9.3%]	6.6% [3.1%, 10.0%]
Symptomatic Deep Vein Thrombosis (DVT)	2.5% [0.3%, 4.7%]	3.5% [1.0%, 6.1%]	4.1% [1.3%, 6.8%]

Event	30 Days	6 Months	12 Months
Pulmonary Embolism (PE)	0.0% [0.0%, 0.0%]	0.0% [0.0%, 0.0%]	0.0% [0.0%, 0.0%]
Myocardial Infarction (MI)	0.5% [0.0%, 1.5%]	0.5% [0.0%, 1.5%]	1.6% [0.0%, 3.3%]
Hematoma	0.5% [0.0%, 2.8%]	*N/A*	*N/A*
Stent Thrombosis	3.5% [1.0%, 6.0%]	9.0% [5.1%, 13.0%]	15.8% [10.7%, 20.9%]

Data presented as (n/N) % where n is the number of subjects experiencing at least 1 event and N is the number of subjects.

Venous Outcomes

The definition of a DVT is any organized clot that is occluded within the deep venous system and results in a lack of flow and a lack of compressibility of the vein. This definition is distinct from catheter-related thrombosis or protein/fibrin deposition that have typically been reported with the use of indwelling central venous catheters and cardiac implantable electronic devices, which are largely asymptomatic, do not occlude the vein, and can be found in the vicinity of the device. Venous events are described below based on CEC adverse event definitions and clinical relevance. The methodologies of categorization of these events are not mutually exclusive. **Table 18** categorizes venous events based upon the CEC definitions of serious and non-serious.

Serious DVTs are those that resulted in either death, life-threatening illness/injury, permanent impairment of a body structure of a body function, inpatient or prolonged hospitalization, or medical or surgical intervention to prevent life-threatening illness or injury or permanent impairment.

Non-serious DVTs are those that did not result in death, life-threatening illness/injury, permanent impairment of a body structure or a body function, inpatient or prolonged hospitalization, or medical or surgical intervention to prevent life-threatening illness or injury or permanent impairment. These may include fibrin sheaths which did not occlude the vein, are largely asymptomatic, and can be found in the vicinity of the device.

Table 18: Deep Vein Thrombosis (DVT) - ITT Population

Event	30 Days % (95% CI) {n/N} [m]	6 Months % (95% CI) {n/N} [m]	12 Months % (95% CI) {n/N} [m]
Non-serious DVT	10.9% (7.0, 16.0) {22/202) [22]	13.9% (9.4, 19.4) {28/202} [30]	13.9% (9.4, 19.4) {28/202} [30]
Non-serious Device Related DVT	6.9% (3.8, 11.4) {14/202}	8.9% (5.4%, 13.7%) {18/202}	8.9% (5.4%, 13.7%) {18/202}

Event	30 Days % (95% CI) {n/N} [m]	6 Months % (95% CI) {n/N} [m]	12 Months % (95% CI) {n/N} [m]
	[14]	[18]	[18]
Non-serious Procedure Related DVT	10.9% (7.0, 16.0) {22/202} [22]	10.9% (7.0, 16.0) {22/202} [22]	10.9% (7.0, 16.0) {22/202} [22]
Serious DVT (or Endpoint DVT)	2.5% (0.8, 5.7) {5/202} [5]	4.0% (1.7, 7.7) {8/202} [8]	4.0% (1.7, 7.7) {8/202} [8]
Serious Device Related DVT	1.5% (0.3, 4.3) {3/202} [3]	2.5% (0.8, 5.7) {5/202} [5]	2.5% (0.8, 5.7) {5/202} [5]
Serious Procedure Related DVT	2.5% (0.8, 5.7) {5/202} [5]	3.0% (1.1, 6.4) {6/202} [6]	3.0% (1.1, 6.4) {6/202} [6]
All DVT **Events** (serious and non-serious, regardless of relation to device or procedure)	27 events	38 events	38 events

Data presented as (95% exact CI) {n/N} [m] where n is the number of subjects experiencing at least 1 event, N is the number of subjects, and m is the total number of events.

Figure 6 below organizes the venous events by clinical relevance. The events were categorized as symptomatic DVT, which are venous events that are occlusive within a deep vein and associated with clinical symptoms, and those that are not. Symptomatic DVTs (or endpoint DVTs) were considered as part of the safety endpoint. Venous events that are not symptomatic are likely the result of fibrin deposition/sheath. Details on gender and treatment are also reported.

There were a total of 38 venous events reported in 36 patients from patients reporting of symptoms and venous duplex surveillance at follow-up visits. Most were found incidentally on follow-up imaging. All of these events were reviewed by an independent Clinical Events Committee and Medical Monitor. There were eight (8) symptomatic DVTs in eight (8) patients that were considered as part of the safety endpoint. However, one (1) was later assessed to be an arterial occlusion in the bypass graft. Symptomatic DVT occurred in 7.5% (4/53) of females and 2.0% (3/147) of males. All 7 symptomatic DVTs resolved.

There were a total of 30 venous events in 28 patients that were not considered symptomatic or occlusive, and most were found incidentally on follow up imaging. One (1) was later assessed to be an arterial occlusion of the SFA and popliteal artery, Venous events occurred in 15.1% (8/53) of females and 12.9% (19/147) of males; 14 patients started on anticoagulation and 13 patients had no additional treatment. All but one (1) of

the venous events resolved within 6 months. The one venous event was resolved by year 2, without any further reintervention.

Overall, there were no significant interventions (e.g., lysis, thrombectomy) used in the treatment of any of the venous events. There was no progression in size, or progression to pulmonary embolism.

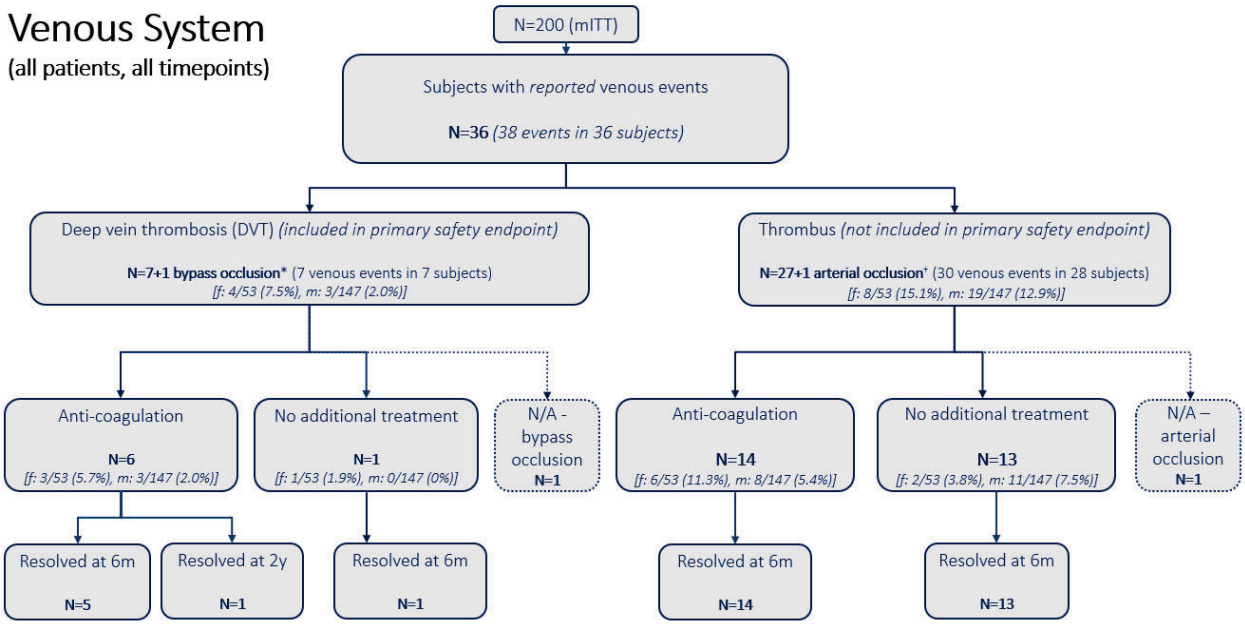

Figure 6: Deep Vein Thrombosis - MITT Accountability

**N=8 events were counted against the primary safety endpoint (i.e., freedom from MAEs at 30 days), however N=1 event was later determined to be a bypass occlusion*
†N=28 events were reported as venous events but not counted against the primary safety endpoint, however N=1 event was an arterial occlusion

Duplex Venous Observation Scale (DVOS)

Duplex Venous Observation Scale was performed at 30 days, 6 months and 12 months, as shown in **Table 19** in the ITT Cohort. The analysis demonstrates a DVOS of 0 for the majority of subjects indicating the vein was patent with no presence of fibrin or thrombus.

Table 19: Duplex Venous Observation Scale - ITT

DVOS	30 Days (N=173[1])	6 Months (N=175)	12 Months (N=171)
0	83.2% (144)	94.3% (165)	96.5% (165)
1	0.6% (1)	1.1% (2)	0.0% (0)
2	1.7% (3)	0.0% (0)	0.6% (1)
3	0.6% (1)	0.0% (0)	0.0% (0)

DVOS	30 Days (N=173[1])	6 Months (N=175)	12 Months (N=171)
4	11.0% (19)	4.0% (7)	2.3% (4)
5	2.9% (5)	0.6% (1)	0.6% (1)

[1]*Missing imaging assessment from the expected ITT Cohort group (202 at 30 days)*

Venous Clinical Severity Scale (VCSS) and Villalta Scale Results

Results for the VCSS scales at baseline and for each visit interval (30 days, 6 months, 12 months, 24 months and 36 months) are summarized in **Table 20**. The VCSS instrument provides a general assessment for patients with chronic venous disease. A negative change from baseline indicates improvement in the parameter assessed. At 30 days, 6 months and 12 months, patients reported less pain. In the patients that have reached the 24- and 36-months follow-up, the pain and varicose veins were improved. However, overall VCSS score at 1 year was 0.3 ± 1.98, indicating on average the study subjects had a decline in their status with regard to their preexisting chronic venous disease.

Table 20: Venous Clinical Severity Score - ITT

Visit	All Available	Change from Baseline (Follow-up – Baseline)
Baseline	0.9 ± 0.89 (202) 1.0 (0,2)	--
30 Day	1.7 ± 2.23 (194) 1.0 (0. 14)	0.7 ± 2.11 (194) 0.0 (-2, 12)
6 Months	1.2 ± 2.08 (189) 1.0 (0, 19)	0.3 ± 1.99 (189) 0.0 (-2, 17)
12 Months	1.3 ± 1.97 (173) 1.0 (0, 12)	0.3 ± 1.98 (173) 0.0 (-2, 11)

Data presented as mean ± SD (N) median (min, max) where N is the number of subjects with available data.

Results for the Villalta scales scores for each visit interval (30 days, 6 months, 12 months, 24 months and 36 months) are summarized in **Table 21**. The Villalta score is used for post-thrombotic syndrome. It combines a patient self-assessment of symptoms and a healthcare assessment of clinical signs of post-thrombotic syndrome. A negative change from baseline indicates improvement in the parameter assessed. At 30 days, 6 months, 12 months, the overall Villalta score showed an improvement. The overall change in score at 1 year was -0.6 ± 3.23. In the patients who had reached 24- and 36-months follow-up, an improvement remains.

Table 21: Villalta Scale - ITT

Visit	All Available	Change from Baseline (Follow-up – Baseline)
Baseline	2.0 ± 3.08 (202) 1.0 (0.17)	--
30 Day	1.7 ± 2.86 (194) 0.5 (0, 19)	-0.4 ± 3.29 (194) 0.0 (-12, 17)
6 Month	1.3 ± 2.37 (189) 0.0 (0, 16)	-0.8 ± 3.16 (189) 0.0 (-14, 13)
12 Month	1.5 ± 2.76 (173) 0.0 (0.17)	-0.6 ± 3.23 (173) 0.0 (-13, 11)

Data presented as mean ± SD (N) median (min, max) where N is the number of subjects with available data.

Stent Graft Separation and Migration

Assessment of Stent Graft Separation and Migration was performed at 30 days, 6 months, 12 months, 24 months and 36 months, as shown in **Table 22**, through differing imaging modalities. One ultrasound detected stent graft separation and migration at the 12-month follow-up visit. One 12-month X-ray detected three (3) migrations (1.8%; 3/169) and one stent separation (0.6%; 1/169). There were no stent graft fractures at 12-months, and no additional separations, migrations, or fractures have been seen in patients who have reached follow-up through 36 months.

Table 22: Stent Graft Separation and Migration via Ultrasound and X-ray - ITT

		30 Days	6 Months	12 Months
Ultrasound	Stent Graft Separation	0.0% (0/192) [0.0%, 1.9%]	0.0% (0/188) [0.0%, 1.9%]	0.6% (1/180) [0.0%, 3.1%]
	Stent Graft Migration	0.0% (0/192) [0.0%, 1.9%]	0.0% (0/188) [0.0%, 1.9%]	0.6% (1/180) [0.0%, 3.1%]
	Stent Graft Separation or Migration	0.0% (0/192) [0.0%, 1.9%]	0.0% (0/188) [0.0%, 1.9%]	0.6% (1/180) [0.0%, 3.1%]
X-Ray	Stent Graft Separation	N/A	N/A	1.8% (3/169) [0.4%, 5.1%]
	Stent Graft Migration	N/A	N/A	0.6% (1/169) [0.0%, 3.3%]
	Stent Graft Separation or Migration	N/A	N/A	1.8% (3/169) [0.4%, 5.1%]

Data presented as % (n/N) [95% CI] where N is the number of subjects with available data.

3. Effectiveness Results

The analysis of effectiveness was based on the 188 evaluable patients at the 12-month time point. The primary effectiveness endpoint was primary patency, defined as freedom from clinically driven target lesion revascularization (CD-TLR) and absence of recurrent target lesion restenosis of >50% diameter reduction by imaging (duplex ultrasound peak systolic velocity ratio of >2.5 or angiography) within the stent or 1cm immediately above or below the treated segment at 12 months. When both imaging modalities are available, angiography takes precedence.

Primary patency at 12 months was 68.1% (128/188). The lower bound of an exact one-sided 97.5% confidence interval is 60.9%. As this is above the prespecified 60.4% threshold of the null hypothesis, the null hypothesis is rejected, and the evidence supports that the primary effectiveness is met. The primary effectiveness outcomes are summarized in **Table 23**. Information on the 12-month primary patency rate with the roll-in cohort is limited by a low number of patients available for analysis (n=18). The primary patency Kaplan-Meier estimate is 57.1% and is within the 95% confidence band of the roll-in cohort.

Table 23: Primary Effectiveness Endpoint, Primary Patency at 12 Months - MITT

	All Subjects	Lower 97.5% Exact Confidence Limit
Absence of CD-TLR[1] and absence of recurrent target lesion diameter stenosis >50%	68.1% (128/188) Patency failures 30% (60/200) CD-TLR: 14% (28/200) [35] PSVR >2.5: 24% (48/200)	60.9% > 60.4%

[1]*Target lesion revascularization performed due to target lesion diameter stenosis >50% (e.g., duplex ultrasound peak systolic velocity ratio of >2.5 or invasive angiography) within the stent or immediately 1cm above or below the treated segment, AND either evidence of clinical or functional ischemia (e.g., recurrent/progressive intermittent claudication, critical limb ischemia) OR recurrence of the clinical syndrome for which the initial procedure was performed.*

In order to meet the criteria for Clinically Driven (CD), the CEC members reviewed the reported TLR source documentation against the CD-TLR definition. To meet the definition of CD-TLR, at least two (2) reviewers must have determined that the event met at least two of the first three criteria. It is noted that the criteria did not need to be the same between the reviewers, only that at least two clinical criteria are met. All TLR are described in **Figure 7** below.

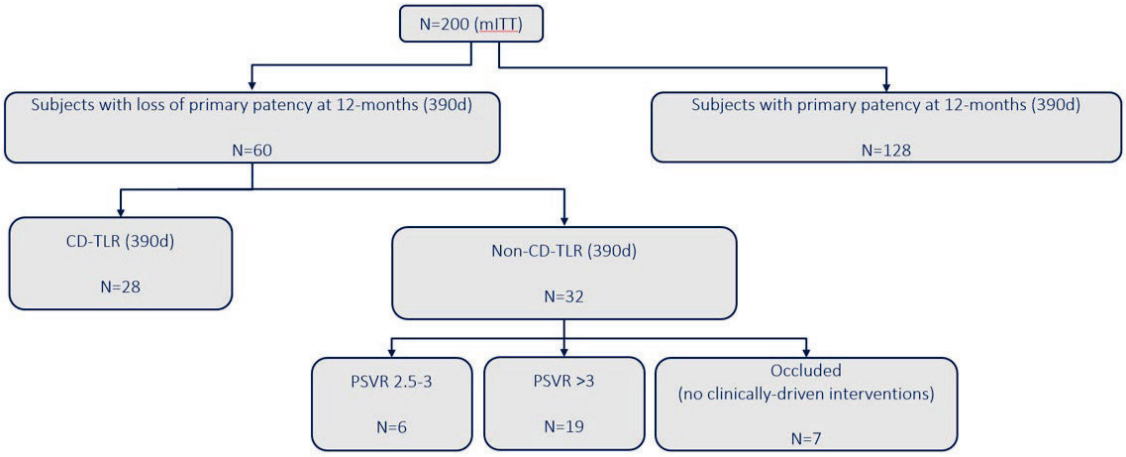

Figure 7: Arterial System at 1 Year - MITT Accountability

4. Secondary Effectiveness Endpoints

All secondary effectiveness analyses were performed on the primary analysis cohort, the MITT analysis set.

Secondary Effectiveness assessments of the MITT group were performed at 30 days, 6 months, 12 months, 24 months and 36 months as shown in **Table 24** and **Table 25**.

Clinical success as defined by subjects showing a ≥1 category improvement in RCC was 92.9% (182/196), and the percentage of subjects with an improvement in RCC remained high through 36 months for those who have completed their 3-years visits. Limb ischemia, identified using the RCC, is reported as change from baseline. A negative value for change from baseline indicates an improvement in RCC.

At each time point in the study, the change from baseline showed RCC improved. At 30 days, 6 months, and 12 months, RCC improved by an average score of 2.7. At 24 months and 36 months, RCC improved by a score of 2.8 and 2.9.

Using Kaplan Meier methodology, the primary patency at 1 year was 72.3%, and the secondary patency at 1 year was 81.8%. Ankle-Brachial Index (ABI) change from baseline on the target limb averaged a 0.4 (±0.25) change at 30 days and a 0.4 (±0.27) change as 12 months. 6 Minute Walk Test (6MWT) change from baseline averaged a 46.8 (±105.29) change at 30 days and a 79.6 (±144.71) change at 12 months.

Table 24: Secondary Effectiveness Endpoints – MITT Population

	30 Days	6 Months	12 Months
Clinical Success	92.9% (182/196)	94.8% (182/192)	97.2% (173/178)

	30 Days	6 Months	12 Months
	[88.3%, 96.0%]	[90.6%, 97.5%]	[93.6%, 99.1%]
Primary Patency*	96.5% [93.9%, 99.0%]	87.9% [83.4%, 92.4%]	72.3% [66.0%, 78.6%]
Secondary Patency*	100.0% [100.0%, 100.0%]	95.4% [92.5%, 98.4%]	89.1% [84.7%, 93.5%]
Major Index Limb Amputations Over Time*	0.0% [0.0%, 0.0%]	0.5% [0.0%, 1.5%]	1.6% [0.0%, 3.3%]

Data presented as % (n/N) Kaplan Meier Estimates rate [95% CI] where N is the number of subjects with available data.

Table 25: Secondary Effectiveness Baseline Comparison - MITT Population

			Baseline	30 Days	6 Months	12 Months
Limb Ischemia: Rutherford Clinical Category (continuous) - MITT						
	All Available		3.3 ± 0.53 (200) 3.0 (3,5)	0.6 ± 1.04 (196) 0.0 (0, 5)	0.5 ± 1.05 (192) 0.0 (0, 5)	0.6 ± 0.96 (178) 0.0 (0, 5)
	Paired Data	Baseline	--	3.2 ± 0.50 (196) 3.0 (3, 5)	3.3 ± 0.53 (192) 3.0 (3, 5)	3.3 ± 0.54 (178) 3.0 (3, 5)
	Paired Data	Follow-up	--	0.6 ± 1.04 (196) 0.0 (0, 5)	0.5 ± 1.05 (192) 0.0 (0, 5)	0.6 ± 0.96 (178) 0.0 (0, 5)
	Paired Data	Change from Baseline (Follow-up – Baseline)	--	-2.7 ± 1.12 (196) -3.0 (-5, 1)	-2.7 ± 1.07 (192) -3.0 (-5, -2)	-2.7 ± 1.05 (178) 0.0 (0, 5)
Ankle-Brachial Index (ABI) - MITT						
Target Limb	All Available		0.61 ± 0.22 (191) 0.60 (0.00, 1.55)	0.99 ± 0.18 (183) 1.00 (0.00, 1.71)	0.99 ± 0.21 (173) 1.00 (0.37, 1.98)	0.95 ± 0.21 (170) 0.97 (0.00, 1.97)
	Paired Data	Baseline	--	0.61 ± 0.22 (178) 0.61 (0.00, 1.55)	0.61 ± 0.22 (169) 0.59 (0.00, 1.55)	0.60 ± 0.22 (166) 0.59 (0.00, 1.55)
	Paired Data	Follow-up	--	0.99 ± 0.18 (178) 1.00 (0.00, 1.71)	0.98 ± 0.21 (169) 1.00 (0.37, 1.98)	0.96 ± 0.21 (166) 0.97 (0.00, 1.97)

			Baseline	30 Days	6 Months	12 Months
	Paired Data	Change from Baseline (Follow-up – Baseline)	--	0.38 ± 0.25 (178) 0.38 (-0.66, 1.20)	0.38 ± 0.24 (169) 0.38 (-0.49, 1.12)	0.36 ± 0.27 (166) 0.37 (-0.74, 1.04)
Contralateral Limb	All Available		0.81 ± 0.26 (187) 0.81 (0.00, 1.63)	0.87 ± 0.24 (181) 0.90 (0.21, 1.88)	0.89 ± 0.24 (170) 0.93 (0.28, 1.97)	0.88 ± 0.25 (163) 0.89 (0.02, 1.97)
	Paired Data	Baseline	--	0.82 ± 0.26 (172) 0.82 (0.00, 1.63)	0.83 ± 0.26 (163) 0.82 (0.00, 1.63)	0.82 ± 0.26 (157) 0.82 (0.00, 1.63)
	Paired Data	Follow-up	--	0.87 ± 0.24 (172) 0.90 (0.21, 1.88)	0.89 ± 0.24 (163) 0.92 (0.28, 1.97)	0.88 ± 0.25 (157) 0.89 (0.02, 1.97)
	Paired Data	Change from Baseline (Follow-up – Baseline)	--	0.05 ± 0.21 (172) 0.04 (-0.44, 1.16)	0.06 ± 0.23 (163) 0.04 (-0.53, 1.25)	0.06 ± 0.28 (157) 0.04 (-1.51, 1.25)
6 Minute Walk Test (6MWT) - MITT						
	All Available		208.8 ± 133.18 (142) 194.5 (18, 800)	259.7 ± 147.84 (131) 229.8 (0, 864)	--	288.4 ± 141.51 (118) 291.5 (0, 1004)
	Paired Data	Baseline	--	213.4 ± 132.63 (130) 199.6 (23, 800)	--	209.8 ± 118.73 (117) 198.0 (23, 650)
	Paired Data	Follow-up	--	260.3 ± 148.26 (130) 230.7 (0, 864)	--	289.4 ± 141.76 (117) 292.0 (0, 1004)
	Paired Data	Change from Baseline (Follow-up – Baseline)	--	46.8 ± 105.29 (130) 30.2 (-270, 427)	--	79.6 ± 144.71 (117) 61.0 (-366, 913)

Categorical variables presented as % (n/N) and continuous variables presented as mean ± SD (N) median (min, max) where N is the number of subjects with available data.

Secondary Effectiveness assessments of the MITT group were performed at 30 days, 6 months, 12 months, 24 months and 36 months as shown in **Table 24** and **Table 25**.

Clinical success as defined by subjects showing a ≥1 category improvement in RCC was 92.9% (182/196), and the percentage of subjects with an improvement in RCC remained high through 36 months for those who have completed their 3-years visits. Limb ischemia, identified using the RCC, is reported as change from baseline. A negative value for change from baseline indicates an improvement in RCC.

At each time point in the study, the change from baseline showed RCC improved. At 30 days, 6 months, and 12 months, RCC improved by an average score of 2.7. At 24 months and 36 months, RCC improved by a score of 2.8 and 2.9.

Using Kaplan Meier methodology, the primary patency at 1 year was 72.3%, and the secondary patency at 1 year was 81.8%. Ankle-Brachial Index (ABI) change from baseline on the target limb averaged a 0.4 (±0.25) change at 30 days and a 0.4 (±0.27) change as 12 months. 6 Minute Walk Test (6MWT) change from baseline averaged a 46.8 (±105.29) change at 30 days and a 79.6 (±144.71) change at 12 months.

Reinterventions

Interventions were classified as TVR, TLR, or CD-TLR, as presented in **Table 26**. TVR and TLR were further classified as lysis or non-lysis procedures. Lysis was defined as the use of thrombolytic drug therapy during the intervention or reporting of thrombolytic techniques by the site. It is noted that some patients may have had multiple procedures, therefore counts may not sum across rows or columns.

Table 26: Reinterventions

	# Events in Interval Up to 30 Days (0-30 days) % (n/N)[m][1]	# Events in Interval 6 Months (31-180 days) % (n/N)[m][1]	# Events in Interval 12 Months (181-390 days) % (n/N)[m][1]	Total Events to 12 Months (390 days) (n/N)[m][1]
All TVR	2% (4/200) [4]	6.5% (13/200) [15]	13% (26/200) [33]	21.5% (43/200) [52]
TVR (excluding lysis only)[2,3]	2% (4/200) [4]	5% (10/200) [12]	13% (26/200) [30]	19% (38/200) [46]
TVR (including lysis only)	0% (0/200) [0]	1.5% (3/200) [3]	1.5% (3/200) [3]	2.5% (5/200) [6]
All TLR	2% (4/200) [4]	6% (12/200) [14]	11.5% (23/200) [29]	19.5% (39/200) [47]
TLR (excluding lysis only)[2,3]	2% (4/200) [4]	4.5% (9/200) [11]	11% (22/200) [26]	16.5% (33/200) [41]
TLR (including lysis only)	0% (0/200) [0]	1.5% (3/200) [3]	1.5% (3/200) [3]	2.5% (5/200) [6]

	# Events in Interval Up to 30 Days (0-30 days) % (n/N)[m][1]	# Events in Interval 6 Months (31-180 days) % (n/N)[m][1]	# Events in Interval 12 Months (181-390 days) % (n/N)[m][1]	Total Events to 12 Months (390 days) (n/N)[m][1]
CD-TLR	1.5% (3/200) [3]	5% (10/200) [12]	9% (18/200) [20]	14% (28/200) [35]

[1] Data presented as % (n/N) [m] where n is the number of subjects experiencing at least 1 event, N is the number of subjects, and m is the total number of events.
[2] Target Vessel Revascularization (TVR) – Any repeat percutaneous intervention (excluding lysis only) or surgical bypass of any segment of the target vessel.
[3] Target Lesion Revascularization (TLR) – A repeat percutaneous intervention (excluding lysis only) or surgical bypass of the target lesion site or immediately 1cm above or below the treated arterial segment.

5. Subgroup Analyses

The following subgroups were assessed for impact on Primary Safety and Primary Effectiveness: gender and region. Please note that the stratification of the study into these smaller cohorts reduces the sample size available to accurately assess estimates and may impact interpretability.

Gender

The subgroup analysis by gender showed that females had a greater risk of primary patency failure at one year compared to males.

Table 27: Primary Patency at 12 Months by Gender - MITT

Subgroup	All Subjects	Lower 97.5% Exact Confidence	P-value
Female	49.0% (24/49)	34.4%	0.001
Male	74.8% (104/139)	66.8%	

Data presented as % (n/N) where N is the number of subjects with available data. P-value based on generalized Fisher's Exact test.

There are multifactorial issues that impact the assessment of study outcomes for the female gender. Further information is available below on the post hoc, multivariate regressions analysis, completed to provide additional information. There are large studies that show that female gender does not contribute to graft failure and reduced patency. It has been hypothesized that reasons for poorer outcomes in women are multifactorial, including anatomical variables (e.g., smaller vessels), presentation with more advanced disease, and biological characteristics that influence the long-term outcomes of revascularization.

Region

Additionally, the analysis showed that primary patency was significantly better in the OUS patients compared with the US patients.

Table 28: Primary Patency at 12 Months by Region - MITT

Subgroup	All Subjects	Lower 97.5% Exact Confidence Limit	P-value
OUS sites	89.4% (42/47)	76.9%	<0.001
US sites	60.1% (86/143)	51.6%	

The US population had higher rates of ISR patients [21.6% (33/153) vs. 4.1% (2/49); p=0.004], a shorter patent length of the above knee popliteal section [79.53 ± 44.2 (146) vs 99.15 ± 53.2 (44); p=0.015], more CFA disease present (9.2% vs 0%; p=0.024), and smaller distal CFA diameters [7.65 ± 1.7 (150) vs. 8.73 ± 1.4 (48); p<0.001]. These lesion characteristics may have contributed to a lower primary patency for the US cohort. Post-hoc multivariate logistic regression analyses, (**Table 29**) were conducted to select the covariates that best explain the variability in primary endpoints.

In summary, it was found that smaller distal CFA diameters, shorter height/heavier weight, longer CTO length and history of smoking were predictors of poor patency. When accounting for these variables, gender became a statistically insignificant predictor. When evaluating the differences between the US and OUS cohorts, each of these predictor variables provided the OUS with an advantage. That is, the European participants were taller and had larger vessels. Therefore, it is uncertain whether outcomes for these cohorts are more directly correlated to anatomic and lesion characteristics. However, with small numbers in these groups, it is difficult to draw definitive conclusions.

Table 29: Odds Ratio Estimates for Patency Model

Odds Ratio Estimates			
Effect	**Point Estimate**	**95% Wald Confidence Limits**	
Region: OUS vs US	0.403	0.154	1.057
Distal CFA Diameter	0.754	0.595	0.954
Height	0.924	0.881	0.968
Weight	1.031	1.005	1.058
CTO Length	1.046	0.999	1.094
Smoking Status (current vs former)	2.707	1.323	5.538

6. Pediatric Extrapolation

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

E. Financial Disclosure

The Financial Disclosure by Clinical Investigators regulation (21 CFR 54) requires applicants who submit a marketing application to include certain information concerning the compensation to, and financial interests and arrangement of, any clinical investigator conducting clinical studies covered by the regulation. The pivotal clinical study included 163 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. SUMMARY OF SUPPLMENTAL CLINICAL INFORMATION

The DETOUR1 Trial was a single-arm, multicenter trial for patients with long-segment femoropopliteal disease. Seventy-eight (78) patients (82 limbs) were enrolled with eight (8) participating centers located in four (4) countries, specifically Latvia, Germany, Poland, and Chile. Eligibility included TASC C and TASC D lesions >10cm. The primary safety endpoint was the 30-day rate of MAE, defined as a composite endpoint of death, CD-TLR, or major target limb amputation. The primary effectiveness endpoint was a 6-month patency, defined as freedom from occlusion, ≥50% diameter stent-graft stenosis, or CD-TLR. CD-TLR was defined as a revascularization in a target vessel with core laboratory-reported occlusion or restenosis ≥50% and ipsilateral symptoms referable to the lesion. CD-TLR was assessed by the independent Medical Monitor. Primary, assisted-primary, and secondary patency rates were also assessed using standard definitions from the Society of Vascular Surgery guidelines document.

The 1-year results from the DETOUR1 Trial show that the DETOUR System is a safe and effective percutaneous treatment option for patients with longer, severely calcified, above-knee femoropopliteal lesions. The rates of technical and procedural success measured during the index procedure were both 96%, with satisfactory delivery and deployment of the device without MAEs in 79 of 82 limbs. Through 1 month, there were no deaths or amputations; the mean 1-month ABI was 0.94±0.20, an increase of 0.29±0.24, compared with the baseline; CD-TLRs occurred in 2 of 81 limbs (3%), and freedom from secondary patency rates were 81% ±4%, 82% ±4%, and 90% ±3%, respectively. Through 1 year, the Kaplan-Meier estimates of freedom from stent graft thrombosis, CD-TLR, and MAE were 84% ±64%, 85% ±64%, and 84% ±64%, respectively. At 1 year, the RCC improved in 77 of 80 limbs (96%), and 65 of 80 (81%) were asymptomatic. Deep vein thrombosis developed in 2 of 79 target limbs (2.5%) through 1 year, both at the femoropopliteal vein level. There were no instances of pulmonary embolism. The overall VCSS and Villalta scores did not change during follow-up.

Key effectiveness and safety endpoints are presented in **Table 30**.

Table 30: DETOUR1 Key Endpoint Results Effectiveness and Safety

	1 Month	3 Months	6 Months	1 Year
Effectiveness outcomes[1]				
Clinical success	76/81 (93.8)	82/82 (100.0)	77/81 (95.1)	77/80 (96.3)
Rutherford Clinical Category				
0. Asymptomatic	60/81 (74.1)	67/82 (81.7)	67/81 (82.7)	65/80 (81.3)
1. Mild claudication	14/81 (17.3)	12/82 (14.6)	8/81 (9.9)	8/80 (10.0)
2. Moderate claudication	2/81 (2.5)	2/82 (2.4)	2/81 (2.5)	4/80 (5.0)
3. Severe claudication	2/81 (2.5)	0/82 (0.0)	3/81 (3.7)	2/80 (2.5)
4. Ischemic rest pain	2/81 (2.5)	0/82 (0.0)	1/81 (1.2)	0.80 (0.0)
5. Minor tissue loss	1/81 (1.2)	0/82 (0.0)	0/81 (0.0)	1/80 (1.3)
6. Major tissue loss	0/81 (0.0)	0.82 (0.0)	0.81 (0.0)	0.80 (0.0)
Ankle-brachial index (ABI)	0.94 ±0.20	0.94 ±0.22	0.93 ±0.24	0.90 ±0.20
Safety outcomes[2]				
MAEs	2/81 (2.5)	4/81 (4.9)	7/81 (8.6)	13/80 (16.3)
Death	0/81 (0.0)	0/81 (0.0)	1/80 (1.3)	1/79 (1.3)
CD-TLR	2/81 (2.5)	4/81 (4.9)	6/80 (7.5)	12/79 (15.2)
Target limb amputation	0/81 (0.0)	0/81 (0.0)	0/80 (0.0)	0/79 (0.0)
MAVEs	4/81 (4.9)	7/81 (8.6)	9/80 (11.3)	14/79 (17.7)
Stent thrombosis	3/81 (3.7)	6/81 (7.4)	8/80 (10.0)	13/79 (16.5)
Clinically apparent distal embolization	0/81 (0.0)	0/81 (0.0)	0/80 (0.0)	0/79 (0.0)
Procedure-related arterial rupture	0/81 (0.0)	0/81 (0.0)	0/80 (0.0)	0/79 (0.0)

	1 Month	3 Months	6 Months	1 Year
Acute limb ischemia	0/81 (0.0)	0/81 (0.0)	0/80 (0.0)	0/79 (0.0)
Bleeding event requiring transfusion	1/81 (1.2)	1/81 (1.2)	1/80 (1.3)	1/79 (1.3)
DVT in target limb	1/81 (1.2)	1/81 (1.2)	2/80 (2.5)	2/79 (2.5)
VCSS	1.1 ±1.6	0.8 ±1.3	0.8 ±1.2	0.8 ±1.4
Villalta score	0.4 ±0.9	0.8 ±1.7	0.5 ±1.0	0.5 ±1.1
Stent fracture	0/81 (0.0)	0.81 (0.0)	0/80 (0.0)	0/79 (0.0)

[1]*Values reported as n/N (%). The denominators reflect the number of limbs with entries for the given follow-up period.*
[2]*Values are reported as n/N (%). The denominator at each time point is equal to the number of limbs (lesions) that reached the lower limit of the follow-up window plus the number of limbs that experienced an event and did not reach the lower limit of the follow-up window.*
Clinical success: limb ischemia improvement by Rutherford Clinical Category (improvement in scale by ≥1 through follow-up.
DVT, Deep vein thrombosis; MAEs, major adverse events; MAVEs, major adverse vascular events; VCSS, Venous Clinical Severity Score.
MAVE through follow-up is defined as stent thrombosis, target limb amputation, clinically apparent distal embolization (defined as causing end organ damage

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

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

XIII. CONCLUSIONS DRAWN FROM PRECLINICAL AND CLINICAL STUDIES

A. Effectiveness Conclusions

The *in vitro* engineering testing conducted on the DETOUR System (consisting of the ENDOCROSS Device and the TORUS Stent Graft and Delivery System) demonstrated that the performance characteristics of the device met the product specifications. The test results obtained from sterilization testing demonstrated that the product can be adequately sterilized and is acceptable for clinical use. The shelf-life testing has established acceptable performance for a labeled shelf life up to 1 year.

The prospective, multi-center, single-arm, international, non-randomized DETOUR2 Clinical Study was designed to evaluate the safety and effectiveness of the DETOUR System for the percutaneous treatment of patients with symptomatic femoropopliteal occlusive disease. The primary effectiveness endpoint was patency at 12 months post-procedure. Patency was defined as the absence of CD-TLR and absence of recurrent target lesion diameter stenosis >50% by imaging (e.g., duplex ultrasound peak systolic velocity ratio [PSVR] of >2.5 within

the stent or immediately 1cm above or below the treated segment). The primary effectiveness endpoint was evaluated against a literature-derived performance goal of 60.4%.

The 12-month primary patency rate in the 188 subjects with evaluable imaging was 68.1% with a lower 97.5% CI of 60.9% which met the PG of 60.4%. Clinical success was demonstrated with sustained improvements in RCC and ABI.

While the overall effectiveness of the DETOUR System was favorable, some uncertainty was observed when analyzed by the subgroups of gender and region. Females had a reduced primary patency at one year compared to males (49% vs. 74.8%). US subjects had a reduced primary patency at one year compared to OUS subjects (60.1% vs. 89.4%). A post-hoc analysis, multivariate regression analysis, identified factors that were better predictors of patency (e.g., vessel size, BMI, lesion characteristics) than gender and region; however, the study was not powered to draw definitive conclusions regarding causality.

B. Safety Conclusions

The biocompatibility and *in vivo* animal testing demonstrated that the associated acute and chronic *in vivo* risks were sufficiently small to support the reasonable assurance of safety of the DETOUR System in its intended clinical use.

In the DETOUR2 trial, 199 treated study subjects were included in the 30-day primary safety analysis. The primary safety endpoint was freedom from Major Adverse Events (MAEs) through 30 days defined as any of the following:

- All-cause mortality
- CD-TLR
- Amputation of the treated limb
- Occlusive-symptomatic deep vein thrombosis
- Pulmonary embolism
- Procedure-related bleeding

The proportion of subjects free from primary safety events was 93.0% with lower 97.5% CI of 88.5%, which met the literature-derived PG of 84%. There were no deaths, amputations of the treated limb, or PE through 30-days.

There were 8 symptomatic DVTs in 8 patients that were considered as part of the safety endpoint and an additional 30 venous events in 28 patients that were categorized as “non-serious” because they were not symptomatic or occlusive, and most were found incidentally on follow up imaging; 14 patients started on anticoagulation and 13 patients had no additional treatment. All but one (1) of the venous events resolved within 6 months. The one venous event was resolved by year 2, without any further reintervention. There were no endovascular interventions (e.g., lysis, thrombectomy) used in the treatment of any of the venous events. Symptomatic DVT rates were higher in females compared with males at 7.5% (4/53) vs 2.0% (3/147), respectively.

C. Benefit-Risk Determination

The probable benefits and risks of the device are based on data collected in a clinical study conducted to support PMA approval as described above. The probable benefits of using the DETOUR System to treat symptomatic femoropopliteal lesions are providing an alternative treatment method to improve blood flow and quality of life of patients who may be suboptimal candidates for surgical or alternative endovascular treatments. The frequency and the types of most adverse events reported through the pivotal clinical study are in alignment with those that might be expected in the studied patient population and therapeutic area. Unlike traditional treatments for arterial disease, the procedure using the DETOUR System introduces an implant into the venous system and therefore adds associated risks (e.g., DVT, PE).

In conclusion, given the available information above, the data support that the probably benefits outweigh the probable risks for using the DETOUR System for percutaneous revascularization in patients with symptomatic femoropopliteal lesions from 200mm to 460mm in length with chronic total occlusions (100mm to 425mm) or diffuse stenosis >70% who may be considered suboptimal candidates for surgical or alternative endovascular treatments.

1. Patient Perspective

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

D. Overall Conclusions

The clinical and non-clinical data in this application support the reasonable assurance of safety and effectiveness of the devices when used in accordance with the indications for use. The results of the prospective, multi-center, single-arm, international, non-randomized clinical study demonstrate that the DETOUR System is safe and effective in the treatment of symptomatic femoropopliteal occlusive disease when used in accordance with the labeling and Instructions for Use.

XIV. CDRH DECISION

CDRH issued an approval order on June 7, 2023. The final clinical conditions of approval cited in the approval order are described below.

1. DETOUR2 Continued Follow-up Study. This study should be conducted per protocol { STP 203 Rev F} (dated 16 March 2020). This study is a prospective, single-arm, multi-center follow-up of the pivotal DETOUR2 trial (G170083) that treated 220 patients at 36 investigational sites. It will evaluate the long-term safety and effectiveness of the DETOUR System. All 197 remaining subjects, active at the end of the 12-month evaluation, will continue to be followed at 24- and 36-months post-procedure.

   Follow-up at the timepoints will include the following assessments: arterial Duplex ultrasound examination to assess stent graft patency and stent-graft separation, venous

Duplex ultrasound to assess for venous events (e.g., deep vein thrombosis), ABI, Rutherford Classification, Venous Clinical Severity Score and Villalta Scale, adverse events, all-cause mortality, target lesion revascularization, target vessel revascularization, major amputation.

2. PTAB1 Study: New-Enrollment Registry Study. The PTAB1 Study is a prospective, single arm, registry-based study designed to evaluate the real-world use of the DETOUR System in treated patients with symptomatic femoropopliteal lesions from 200 mm to 460 mm in length with chronic total occlusions (100 mm to 425 mm) or diffuse stenosis > 70% who may be considered suboptimal candidates for surgical or alternative endovascular treatments. The study will be implemented within the Society for Vascular Surgery Patient Safety Organization Vascular Quality Initiative registry sites in the United States (protocol received interactively on June 5, 2023). A maximum of 450 subjects will be enrolled with a target study population of at least 200 evaluable female and 200 evaluable male participants at the 12-month post-procedure follow-up visit.

   Follow up visits/assessments will be completed at 1, 12, 24-, 36-, 48-, and 60-months post-procedure.

   The primary effectiveness endpoint of freedom from clinically-driven target lesion revascularization (CD-TLR) as determined by an independent imaging Core Lab and the primary safety endpoint of freedom from a major adverse event (MAE) at 30 days post-procedure, defined as death, major amputation, and CD-TLR will be evaluated. Key secondary endpoints to be evaluated are:
   - Perioperative and long-term:
     - Major amputation
     - All-cause mortality
     - Procedure-related Myocardial infarction
     - Deep Vein Thrombosis and/or Pulmonary Embolism
     - Incidental venous thrombosis or thrombus
     - Amputation-free survival
     - Major Adverse Limb Events (MALE)
     - Assisted patency
     - Secondary patency
   - Perioperative only:
     - Procedure duration
     - Length of stay (from Index procedure to discharge)
     - Discharge status

   In addition, vascular imaging (arterial and venous) sub-study of the first 55 females and 55 males enrolled will be completed. The sub-study will include Duplex imaging at 1-, 12-, 24-, and 36-months post-procedure to assess the endpoints of graft primary patency and venous thrombus within the vein containing the graft. Key endpoints to be evaluated are:
   - Patency is defined as the absence of clinically driven target lesion revascularization (CD-TLR) and absence of recurrent target lesion diameter

stenosis >50% by imaging (e.g., duplex ultrasound peak systolic velocity ratio peak systolic velocity ratio [PSVR] of >2.5 or as measured by invasive angiography) within the stent or immediately 1 cm above or below the treated segment.
- Venous thrombus within the vein containing the graft (i.e., thrombus or fibrin within the vein observed on imaging without symptoms)
- Symptomatic DVT
- Occlusive DVT
- Non-occlusive DVT

The study endpoint analyses will be summarized with descriptive statistics. The primary effectiveness endpoint will be analyzed by a Kaplan-Meier analysis, with censoring performed at the last informative time point. The primary safety endpoint will be presented in tabular fashion with the number of patients, patients with events, and patients evaluable at baseline (day 0). The percentage of patients with events will be provided.

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

XV. APPROVAL SPECIFICATIONS

Directions for use: See device labeling.

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

Post-approval Requirements and Restrictions: See approval order.