Summary of Safety and Effectiveness Data (SSED)

I. GENERAL INFORMATION

Device Generic Name:	Stent, Superficial Femoral Artery
Device Trade Name:	Supera® Peripheral Stent System
Device Product Code:	NIP
Applicant's Name and Address:	IDEV Technologies Inc. 253 Medical Center Blvd. Webster, Texas 77598
Date of Panel Recommendation:	N/A
Premarket Approval Application (PMA) Number:	P120020
Date of FDA Notice of Approval:	March 28, 2014

II. INDICATIONS FOR USE

The Supera® Peripheral Stent System is indicated to improve luminal diameter in the treatment of patients with symptomatic *de novo* or restenotic native lesions or occlusions of the superficial femoral artery (SFA) and/or proximal popliteal artery, with reference vessel diameters of 4.0 to 6.5 mm, and lesion lengths up to 140mm.

III. CONTRAINDICATIONS

The Supera® Peripheral Stent System is contraindicated in:

- patients who are judged to have a lesion that prevents complete inflation of an angioplasty balloon or proper placement of the stent or stent delivery system
- patients who cannot receive antiplatelet or anticoagulation therapy. Based on in vivo thrombogenicity testing, the device should not be used in patients who cannot be anticoagulated as there may be some thrombus formation in the absence of anticoagulation.

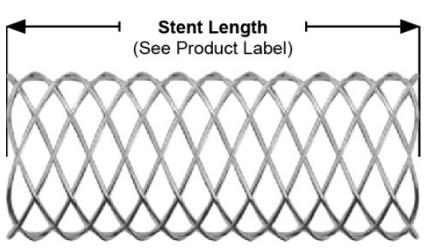
IV. WARNINGS AND PRECAUTIONS

The warnings and precautions can be found in the Supera® Peripheral Stent System labeling (Instructions for Use).

V. DEVICE DESCRIPTION

The Supera Peripheral Stent System consists of a closed end, braided self-expanding stent made of Nitinol (nickel-titanium alloy) wire material that is premounted on a 6Fr or 7Fr delivery system. The stent does not include radiopaque markers.

The over-the-wire (OTW) stent delivery system is compatible with a 0.014" or a 0.018" guide wire and comes in lengths of 80cm and 120cm (6Fr) and 120cm (7Fr). The delivery system includes a reciprocating mechanism (Stent Driver) that incrementally moves the stent distally out of the outer sheath. This motion allows for the distal end of the stent to first come in contact with the targeted vessel, setting the distal reference point, and continues to feed the stent out of the sheath as the target wall is exposed by the proximal movement of the catheter. This stent deployment is achieved by the reciprocation of the Thumb Slide located on the Handle. On the final stroke, the Deployment Lock is toggled and the last deployment stroke is made.



Stent Diameter	Reference Vessel Diameter
4.5mm	4.0-4.5mm
5.50mm	4.6-5.5mm
6.50mm	5.6-6.5mm

Figure 1: Supera Stent (8)

The stents are labeled based on the outer stent diameter. A stent should initially be chosen such that its labeled diameter matches the reference vessel diameter proximal and distal to the lesion, as shown in Figure 1. Final stent selection should be confirmed after lesion pre-dilation: if possible, the stent diameter should match the prepared lesion diameter 1:1. Due to the mechanical behavior of the woven Supera stent, the stent should not be oversized by more than 1 mm relative to the RVD. This ensures optimum deployment of the Supera stent, maximizing radial strength and assisting in accurate stent length deployment. Choosing a labeled diameter to match the reference vessel diameter, then appropriately preparing the vessel to match that stent's outer diameter will result in a stent that is properly sized to the vessel.

The Supera stent is provided in multiple lengths and diameters. Table 1 lists the available stent diameters and lengths for the Supera Peripheral Stent System.

Table 1: Supera Peripheral Stent System Product Specifications

Labeled Stent Diameter (mm)	Nominal Stent Length (mm)	Catheter Outer Sheath Diameter	
		6F	7F
4.5	20, 30, 40, 60, 80, 100, 120	2.00mm, 0.079 inches	2.54mm, 0.100 inches
5.5	20, 30, 40, 60, 80, 100, 120, 150		
6.5	20, 30, 40, 60, 80, 100, 120, 150		

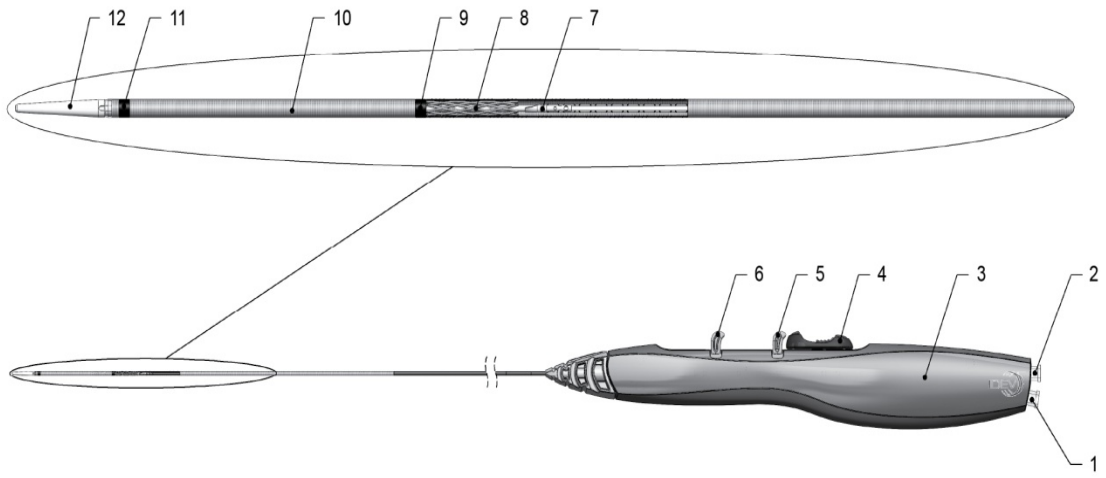


Figure 2: Supera® Peripheral Stent System

Part Number	Part Name	Description/Function
1	Sheath Flush Port	• Used to flush the central lumen of the device
2	Guidewire Flush Port	• Used to flush the guidewire lumen
3	Handle	• Used to control Stent (8) deployment and delivery
4	Thumb Slide	• Advances the Stent (8) out of the Outer Sheath (10) while the Outer Sheath moves in the opposing direction in a de-coupled fashion • Connected internally to the Stent Driver (7)
5	System Lock	• Prevents premature Stent (8) deployment
6	Deployment Lock	• Prevents Stent (8) detachment from the device when locked • Allows final separation of the Stent from the device when unlocked
7	Stent Driver	• Pushes the Stent out of the distal end of the Outer Sheath (10)
8	Stent	• Made of six closed-end interwoven nitinol wires • Constrained to three times its nominal length within the Outer Sheath (10)
9	Stent Length Marker	• Together with the Distal Sheath Marker (11), identifies nominal Stent (8) length and adequate lesion coverage prior to Stent deployment • Embedded in the Outer Sheath (10)

Part Number	Part Name	Description/Function
		• Radiopaque
10	Outer Sheath	• Constrains the Stent (8) until delivery • Moves in the opposite direction of Stent deployment
11	Distal Sheath Marker	• Together with the Stent Length Marker (9), identifies nominal Stent (8) length and adequate lesion coverage prior to Stent deployment • Denotes the distal end of the Outer Sheath (10) • Embedded in the Outer Sheath • Radiopaque
12	Catheter Tip	• Provides an atraumatic guide for catheter advancement along the guidewire • Moves correspondingly with Thumb Slide (4) actuation • Located at the distal end of the catheter shaft • Attached directly to the Stent Driver (7) • Radiopaque

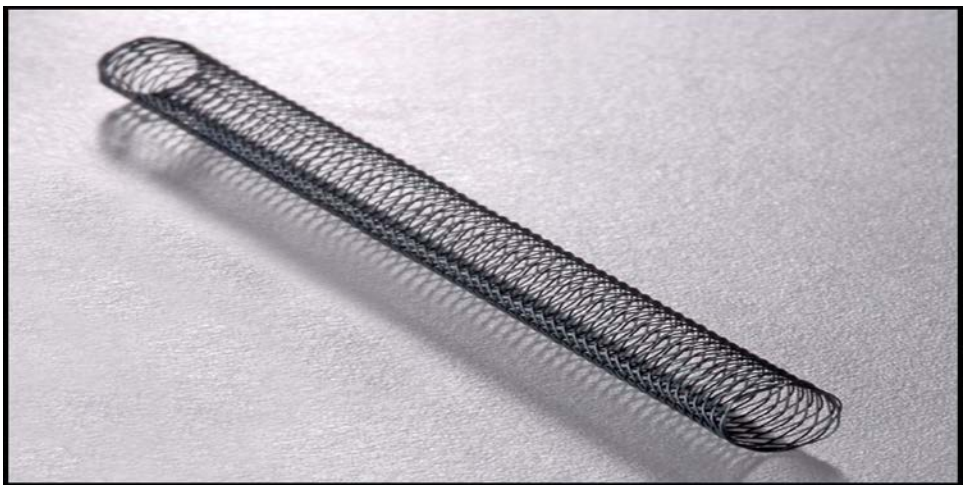


Figure 3: Supera® Stent

VI. ALTERNATIVE PRACTICES AND PROCEDURES

Alternative practices and procedures for treatment of atherosclerotic disease of the superficial femoral and proximal popliteal arteries include:

- Non-invasive lifestyle modifications (e.g., exercise, weight control, cessation of smoking) and drug therapy;
- Minimally invasive endovascular intervention (e.g., balloon angioplasty, stent placement using other FDA approved peripheral stents, and atherectomy); or
- Surgical bypass

Each alternative has its own advantages and disadvantages. A patient should fully discuss those alternatives with his/her physician to select the method that best meets expectations and lifestyle.

VII. MARKETING HISTORY

Currently, the Supera Peripheral Stent System is commercially available outside the US (OUS), including Europe, Canada, and the Asia Pacific region. The Supera Peripheral Stent System for the treatment of lesions in the peripheral arteries (including SFA and PPA) has been available OUS since July 2007. The same device labeled as the Supera Biliary Stent System has been commercially available in the United States and its territories as a biliary stent since January 2008. No products have been withdrawn from the market in any country for any reason.

VIII. POTENTIAL ADVERSE EFFECTS OF THE DEVICE ON HEALTH

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

- Abrupt stent closure
- Allergic reaction (contrast medium; drug; stent material)
- Amputation or limb loss
- Aneurysm or pseudoaneurysm in vessel or at vascular access site
- Angina or coronary ischemia
- Arrhythmia (including premature beats, bradycardia, atrial or ventricular tachycardia, atrial or ventricular fibrillation)
- Arteriovenous fistula
- Bleeding complications from anticoagulant or antiplatelet medication requiring transfusion or surgical intervention
- Death
- Detachment of a system component or implantation in an unintended site
- Embolization, arterial or other (e.g. air, tissue, plaque, thrombotic material, or stent)

- Fever
- Hematoma or hemorrhagic event, with or without surgical repair
- Hypertension/Hypotension
- Infection, local or systemic, including bacteremia or septicemia
- Ischemia requiring intervention (bypass or amputation of toe, foot, or leg)
- Ischemia or infarction of tissue or organ (e.g., occlusion of SFA/PPA or distal vasculature)
- Myocardial Infarction
- Pain (leg, foot, and/or insertion site)
- Partial stent deployment
- Pulmonary embolism
- Renal failure insufficiency secondary to contrast medium (with or without treatment including dialysis)
- Restenosis of vessel in stented segment
- Shock
- Stent malapposition or migration, which may require emergency surgery to remove stent
- Stent strut fracture
- Stent thrombosis or occlusion
- Stroke
- Thrombosis/occlusion at the puncture site, treatment site or remote site
- Transient ischemic attack
- Venous Thromboembolism
- Vessel dissection, perforation or rupture
- Vessel spasm or recoil
- Worsening claudication or rest pain

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

IX. SUMMARY OF PRECLINICAL STUDIES

A. Biocompatibility

Biocompatibility testing was conducted on the Supera® Peripheral Stent System in accordance with applicable Good Laboratory Practices (21 CRF §58) and ISO 10993-1: 2003 *Biological Evaluation of Medical Devices.* The Supera® stent was classified per ISO 10993-1, *Biological Evaluation of Medical Devices* as an implant device in permanent contact (> 30 days) with blood. The Supera® Peripheral Stent System (delivery system only) was classified as an externally

communicating device in limited contact (< 24 hrs) with circulating blood. All testing was conducted on sterilized product.

A summary of the biocompatibility testing conducted can be found in **Table 2** below.

Table 2: Biocompatibility Testing

Test Performed	Test Description	Stent	Delivery System (7Fr)	Delivery System (6Fr)	Results
Cytotoxicity	ISO MEM Elution Assay with L-929 Mouse Fibroblast Cells	X	X	X	Non-toxic
Sensitization	ISO Guinea Pig Maximization	X	X	X	Non-sensitizing
Irritation	ISO Intracutaneous Reactivity	X	X	X	Non-irritating
Pyrogenicity	USP Material Mediated Pyrogenicity	X	X	X	Non-pyrogenic
Acute Systemic Toxicity	ISO Systemic Toxicity Study	X	X	X	Non-toxic
Subchronic Toxicity	Rat Repeat Parenteral Dosing Extract Study – 2 Week		N/A	N/A	Non-toxic
Chronic Toxicity	Rat Chronic Toxicity Study Following Subcutaneous Implantation – 13 Week	X	N/A	N/A	Non-toxic
Implantation	ISO Muscle Implantation Study – 4 Week	X	N/A	N/A	Stent Slight irritant[1]
	ISO Muscle Implantation Study – 26 Week	X	N/A	N/A	Stent Slight irritant[1]

Test Performed	Test Description	Stent	Delivery System (7Fr)	Delivery System (6Fr)	Results
Hemocompatibility	ASTM Hemolysis Study (Direct and Indirect Contac)	X	X	X	Non-hemolytic.
	In vivo Thromboresistance Study – Jugular Vein	N/A[1]	X	X	Delivery System: In the absence of anticoagulation, severe levels of thrombus were seen with some samples. However, with anticoagulation no thrombus was seen.
	Complement Activation Assay C3a and SC5b-9	X	X	X	Not a complement activator
Genotoxicity	Bacterial Reverse Mutation Study	X	N/A	N/A	Non-mutagenic
	Mouse Lymphoma Assay	X	N/A	N/A	Non-mutagenic
	Mouse Peripheral Blood Micronucleus Study	X	N/A	N/A	Non-genotoxic

[1]Also evaluated as a part of the animal studies outlined in Section D, below

Irritation and stent thrombogenicity were evaluated as part of other *in vivo* studies conducted to evaluate the safety and effectiveness of the device in a vascular implant location, as described in Section D, below. These additional animal studies demonstrated a lack of tissue irritation or thrombus formation when stents were implanted in a clinically-relevant vascular implant location.

The omission of carcinogenicity testing was supported by information regarding the starting materials and processing of the finished device and toxicity data from the literature.

The information provided demonstrates that the Supera® Peripheral Stent System is biocompatible.

B. *In vitro* Product Testing

In vitro bench testing to support the Supera® Peripheral Stent System was developed based on the device risk assessment and is consistent with FDA *Non-Clinical Tests and Recommended Labeling of Intravascular Stents and Associated Delivery Systems*, April 18, 2010.

The relevant *in vitro* tests outlined in the guidance document and included in support of the Supera® devices are summarized in **Table 3** below. Unless otherwise specified, all test units were sterilized using a validated Ethylene Oxide sterilization process.

A summary of the tests performed can be found in **Table 3** below.

Table 3: Summary of *in vitro* Product Testing

Test	Clinical or Functional Relevance	Samples Tested	Acceptance Criteria	Summary of Results
Material Characterization				
Material Composition (Stent)*	Characterize the stent material composition to ensure it is acceptable for the intended use.	Stent wire raw material, 2 sizes, 8 lots Stents, all offered diameters, minimum and maximum lengths	ASTM F2063-05	The stent material conforms to implant material standards.
Shape, Memory & Elasticity	The stent must be in its austenitic phase at body temperature to behave superelastically.	Stents, all offered diameters, various lengths	A_f must fall within stent specification range of 10°C -21°C.	Stents were tested and met established specifications for austenitic finish temperature and the stent exhibits expected shape memory properties.
Corrosion Resistance	The stent must resist corrosion following implantation.	Stents, all offered diameters, various lengths, deployed from 6Fr & 7Fr delivery systems	Breakdown potential of 600mV or better per ASTM F2129-08.	The stent met established specifications for corrosion resistance based on testing per ASTM F2129-08.

<table>
<tr><th>Test</th><th>Clinical or Functional Relevance</th><th>Samples Tested</th><th>Acceptance Criteria</th><th>Summary of Results</th></tr>
<tr><td>Fretting Corrosion</td><td>The stent must resist corrosion following implantation due to wear of mated surfaces when overlapped with another stent.</td><td>Stents, various diameters and lengths, deployed from 6Fr & 7Fr delivery systems</td><td>Breakdown Potential ≥ 600 mV</td><td>The stent met the established criteria for fretting corrosion following accelerated durability testing in an overlapped configuration.</td></tr>
<tr><td colspan="5">Stent Dimensional and Functional Attributes</td></tr>
<tr><td>Dimensional Verification</td><td>The stent diameter must be uniform to achieve adequate wall apposition.</td><td>Stents, at the minimum and maximum diameters and lengths (four corners of stent size matrix) deployed from 6Fr & 7Fr delivery systems</td><td><table><tr><th>Stent Inner Diameter (ID) (mm)</th><th>Stent Lengths (mm)</th><th>ID spec. (MM)</th></tr><tr><td>4.0</td><td>20, 40, 60, 80, 100, 120, 150</td><td>± 0.5</td></tr><tr><td>5.0</td><td>20, 40, 60, 80, 100, 120, 150</td><td>± 0.5</td></tr><tr><td>6.0</td><td>20, 40, 60, 80, 100, 120, 150</td><td>± 0.5</td></tr></table></td><td>The stent dimensions were verified post-deployment and met the established acceptance criteria.</td></tr>
<tr><td>Percent Surface Area of Stent</td><td>The metal coverage of the stent must provide sufficient vessel wall contact to help maintain patency.</td><td>Stents, at the minimum and maximum diameters and lengths (four corners of stent size matrix)</td><td>Stents were characterized for information only</td><td>The Percentage Metal Coverage was calculated.

4.5mm: 28% to
6.5mm: 31%<table><tr><th>Stent Size</th><th>Jedwab Method</th><th>Physical Measurement</th></tr><tr><td>4.5 mm</td><td>30%</td><td>28%</td></tr><tr><td>5.5 mm</td><td>31%</td><td>25%</td></tr><tr><td>6.5 mm</td><td>31%</td><td>24%</td></tr></table></td></tr>
</table>

Test	Clinical or Functional Relevance	Samples Tested	Acceptance Criteria	Summary of Results
Foreshortening	The stent must exhibit minimal foreshortening to assure accurate stent deployment and predictable deployed stent length for the user.	All stent diameters and lengths	Change in length for Supera stent between pre-loading into delivery system and post delivery from delivery system must be minimal. Change in length for Supera stent between constrained in delivery system and deployed from delivery system was characterized for information.	Mean change in length for Supera stent between pre-loading into delivery system and post delivery from delivery system – 0.43% across all stent sizes (range 0.00% - 2.38%). Change in length for Supera stent between constrained in delivery system and deployed from delivery system has been characterized, as follows: • 4.5mm: 57.6% across all stent lengths (range 56.4% - 60.1%) • 5.5mm: 60.4% across all stent lengths (range 57.1% - 62.0%) • 6.5mm: 63.2% (range 61.8% - 64.6%)
Stent Integrity	Post deployment the stent must be free of defects or cracks that may affect long-term performance outcomes.	Stents, at the minimum and maximum diameters and lengths (four corners of the stent matrix) deployed from 6Fr & 7Fr delivery systems	No cracks or surface defects under 10x light microscopy.	Stents were tested and met the established acceptance criteria.

Test	Clinical or Functional Relevance	Samples Tested	Acceptance Criteria	Summary of Results
Radial Outward Force	To characterize the outward force produced by the stent as a function of diameter and ensure the outward force is acceptable for the intended use.	Stents, all offered diameters, various lengths	Stents were characterized for information only:	Radial resistive force at nominal diameter 0.22 – 0.32 N/mm Radial outward Force at nominal diameter; 0.14 – 0.24N/mm Radial Stiffness 0.44 – 0.52Nmm / mm
Mechanical Properties	Characterize the stent materials mechanical properties to ensure they are acceptable for the intended use.	Stents, all offered diameters, minimum and maximum lengths	ASTM F2063-05	The stent material conforms to implant material standards ASTM F2063-05 for material properties.
Strain and Fatigue Analysis/Finite Element Analysis (FEA)	To calculate strains that the stent experiences during deployment and *in vivo* conditions. To ensure the stent does not experience unreasonable strains for the material or the intended use.	Computational model of 4.5mm and 6.5mm diameter stents	Fatigue Safety factor >1 over 10-year simulated implant life for the following conditions: - Pulsatile (including overlapped stents, stents deployed in elongated and compressed conditions and wire diameter tolerance effects) - Axial compression (including overlapped stents) - Bending (including overlapped stents) - Walking (compound axial compression with bending) - Stair-climbing (compound axial compression with bending, stent deployed in elongated conditions and stents with pre-strain due to processing)	Stents were tested and met the established acceptance criteria. All Fatigue Safety Factors > 1.0

Test	Clinical or Functional Relevance	Samples Tested	Acceptance Criteria	Summary of Results
Accelerated Durability Testing- radial pulsatile loading	To evaluate fatigue analysis and failure modes on the stent during implant life in simulated arterial conditions, such as fretting, abrasion, wear and fracture.	Non-overlapped and overlapped configurations: 4.5mm and 6.5mm diameter stents, deployed from 6Fr & 7Fr delivery systems	No type III, IV or V fractures for 10 years simulated use for pulsatile fatigue, including overlapped stents.	Stents were tested and met the established acceptance criteria.
Accelerated Durability Testing – multi-modal loading	To evaluate fatigue analysis and failure modes on the stent during implant life in simulated physiologic conditions, such as fretting, abrasion, wear and fracture.	Overlapped configuration: 4.5mm and 6.5mm stents deployed from 6Fr & 7Fr delivery systems	No type III, IV or V fractures for 10 years simulated use for the following conditions: - Bending, (including overlapped stents) - Axial compression, (including stents deployed in elongated / compressed conditions, and overlapped stents) - Torsion - Walking (compound axial compression with bending, including overlapped stents) - Stair climbing (compound axial compression with bending, including overlapped stents)	Stents were tested and met the established acceptance criteria.
MR Compatibility	To evaluate the MRI safety and compatibility of the implantable stent and ensure that the stent is not affected by scanning at 1.5 Tesla and 3.0 Tesla field strengths.	Stents, all offered diameters, various lengths	The presence of the stent must not pose an additional unacceptable risk to patients when subjected to 1.5T and 3.0T magnetic fields.	Test results demonstrate the stent does not pose additional risk to patients and may be labeled MR Conditional according to ASTM 2503-05.

Test	Clinical or Functional Relevance	Samples Tested	Acceptance Criteria	Summary of Results
Radiopacity	Stent must be visible using angiographic imaging.	Stents, all offered diameters, various lengths	Stent visibility was scored on a scale of 1-10, with 10 being excellent. Scored performance must be $\geq$ 6 out of 10 to pass.	Radiopactiy was evaluated by physicians during animal studies and met the established acceptance criteria.
Crush Resistance	The stent must resist localized compression force and return to its original shape.	Stents, all offered diameters, various lengths	Stent must be able to withstand crushing to 1mm less than nominal diameter without permanent deformation. For information only: 4.5mm stent compressed 31% (2.05mm) = 38.7N 5.5mm stent compressed 31% (2.40mm) = 36.8N 6.5mm stent compressed 31% (2.70mm = 37.1N	Stents were tested and met the established acceptance criteria.
Kink Resistance	The stent must be able to reach a radius of curvature suitable for the intended use without kinking.	Stents, minimum and maximum diameters and lengths (four corners of stent matrix) deployed from 6Fr & 7Fr delivery systems	Stent must be able to resist kinking for all radii greater than or equal to 20mm. Kink radii < 2.2mm for all stent sizes.	Stents were tested and met the established acceptance criteria.

Test	Clinical or Functional Relevance	Samples Tested	Acceptance Criteria	Summary of Results
Delivery System Dimensional & Functional Attributes				
Crossing Profile	To verify the maximum diameter of the stent delivery system and assure compatibility with the recommended sheaths.	6Fr & 7Fr delivery systems	Catheter can be inserted and withdrawn through 6Fr / 7Fr Introducers without sacrificing catheter integrity For information only: The 6Fr outer sheath max outside diameter = 2mm or 0.079” The 7Fr outer sheath max outside diameter = 2.54mm or 0.100”	Catheters were tested and met the established acceptance criteria.
Deployment Force	Measure the force required to deploy the stent and verify it meets specifications based on the intended use.	6Fr & 7Fr delivery systems with stents at minimum and maximum diameters and lengths (4 corners of stent size matrix)	Force to deploy stent is less than 9 lbs.	Devices were tested and met the established acceptance criteria.
Deployment Accuracy	The delivery catheter must deploy the stent with accuracy at the target location based on the intended use.	6Fr & 7Fr delivery systems with stents at the minimum and maximum diameters and lengths (4 corners of stent size matrix)	The system must deploy the stent to within +/- 3mm of distal target location, and to a deployed length of +/- 10% nominal stent length.	Devices were tested and met the established acceptance criteria.
Catheter Bond Strengths*	Verify the delivery catheter bond strengths meet specifications based on the intended use.	6Fr & 7Fr delivery systems	Outer sheath to distal end cap > 8.1lbs; Bonds within handle (n=5) > 3.4lbs; Ratchet to catheter shaft >1.7lbs; Tip assembly > 1.3lbs, Slides to catheter shaft >2.25lbs; Slides to hypotube >7.1lbs	Catheters were tested and met the established acceptance criteria.

Test	Clinical or Functional Relevance	Samples Tested	Acceptance Criteria	Summary of Results

Test	Clinical or Functional Relevance	Samples Tested	Acceptance Criteria	Summary of Results
Catheter Flexibility	To verify the stent delivery system is able to flex and track around a bend radius based on the intended use.	6Fr & 7Fr delivery systems	The system can navigate simulated anatomy with a radius of curvature of 5.0mm at inner surface (9.05mm at centerline) and deploy stent per IFU.	Systems were tested and met the established acceptance criteria.
Torque Strength	Characterize the ability of the delivery catheter to withstand torsional forces expected during the intended use.	6Fr & 7Fr delivery systems	The system shall maintain the ability to deliver a stent with the handle rotated up to and including 360^{o} clockwise and counter clockwise.	Systems were tested and met the established acceptance criteria.

* A subset of the tests in this category were not conducted using sterilized product, but additional data on sterilized product were provided to assess the relevant attributes.

C. Sterilization, Packaging & Shelf Life

Sterilization

The Supera® Peripheral Stent System is Ethylene Oxide (EO) sterilized and meets a sterility assurance level (SAL) of 10^{-6}. Validation and annual revalidation are completed based on the standards in ISO 11135-1: 2007 *Sterilization of health care products – Ethylene oxide – Part 1: Requirements for development, validation and routine control of a sterilization process for medical devices Method B: Conservative determination of lethal rate of the sterilization process – overkill approach.*

Packaging & Shelf Life

Packaging qualification testing was performed on the Supera® Peripheral Stent System which is packaged in a preformed tray, and sealed in a Tyvek pouch. A shelf life of 2 years has been established for the Supera® Peripheral Stent System based on product and package shelf life testing.

D. Animal Studies

The Supera® Peripheral Stent System was subjected to a series of sub-chronic and chronic animal studies. Two (2) *in vivo* studies were performed to demonstrate performance and safety of the Supera® Peripheral Stent System. Both studies were conducted in accordance with Good Laboratory Practices (GLP) per 21 CFR §58. **Table 4** below provides a summary of the *in vivo* animal studies performed with the Supera® Peripheral Stent System.

Table 4: Summary of Pre-Clinical Animal Studies

Study Objective	Study Design	Relevant Findings
GLP Dog Study: To evaluate relative thromboresistance of the material *in vivo*.	Supera stents were placed in the iliac arteries of six dogs. At the end of the study, each device was evaluated for thrombus formation as well as tissue samples from the implant site.	No thrombus formation or significant tissue damage was noted at or near any of the implant sites after one and three months of implantation. All stents were found to be well adhered to the vessel wall with no signs of migration from the original site. There were no signs of vessel occlusion noted at any of the implant sites.
GLP Porcine Study: To assess the safety of the Supera stent system at multiple time points in the porcine model and to evaluate the acute performance (deliverability, usability, etc.) by multiple operators.	Fourteen Yucatan pigs were used in the GLP study. Animals were assigned to the 30, 90, and 180 Day time points. The animals underwent a single interventional procedure on Day 0 in which stents were implanted with 6Fr and 7Fr delivery systems (n=10 each) in bilateral iliac arteries (1 stent per vessel). Five animals were euthanized on Days 30 and 90 and four animals at the 180 day time-point and subjected to a comprehensive necropsy and the iliac arteries were collected. Seven stented arteries at each time point were processed for histopathologic evaluation and three stented arteries at the 30 and 90 day time point were used for SEM assessment of endothelialization.	There were no dissections or perforations. All animals survived to their scheduled endpoint and there were no clinical health or necropsy issues at the 30, 90, and 180 day time points. Angiography prior to necropsy showed minimal in-stent neointima with a group average late lumen loss of 1.1mm - 1.2mm and <20% stenosis. Histopathological assessment demonstrated no adverse effect with respect to lumen size, neointimal proliferation, or degree of stenosis at either time point. There was a small progression of neointima and stenosis over time (up to 90 days) but stenosis was on average minimal <16%. There was negligible injury, inflammation, neointimal fibrin, and adventitial fibrosis at all time points. After 30, 90, and 180 days, the stent was interpreted to have good healing characteristics. Endothelialization was near complete by Day 90 and was completely confluent with no cellular gaps. These data are interpreted to reflect a favorable response to implantation. Acute performance was similar for the 6Fr and 7Fr delivery systems with respect to device delivery, deployment, and radiopacity. The stent delivery catheters allowed for good portioning control while deploying the stent.

Study Objective	Study Design	Relevant Findings
Non-GLP Porcine Study: To validate the acute safety and operational characteristics (e.g. trackability, ergonomics, ease of use, etc.) of the 7Fr Supera Stent System per Product Specification PS00008.	This was an acute study at a single time-point using 3 pigs with 7 stents implanted, 4x40mm, 5x150mm, 4x80mm, 4x60mm, 5x60mm, 4x120mm, 5x40mm. Stents were delivered from the 7Fr Supera Stent System. The animals underwent a single interventional procedure and were terminated upon completion of implantation.	Analysis was user-based ranking on critical functional attributes. The values for all scored metrics were passing. The stents were successfully deployed, and passed the deployment criterion. Lumen flush times for all 7 samples were less than 1 second. This metric passes.
Non-GLP Porcine Study: To validate the acute safety, effectiveness, and operational characteristics (radiopacity, trackability, ease of use, etc) of the 6Fr Supera Stent System per Product Specification PS00009.	This was an acute study where three (3) physicians deployed 22 stents into four (4) pigs. Stent sizes deployed were: 6x200, 4x150, 7x100, 4x150, 7x40, 4x40, 5x40, 5x60, 6x80, 6x200, 7x40, 7x100, 6x200, 7x40, 4x40, 4x40, 5x40, 5x40, 6x40, 6x40, 4x150, 7x100. The animals underwent a single interventional procedure and were terminated upon completion of implantation.	Analysis was user-based ranking on critical functional attributes. The values for all scored metrics were passing. Lumen flush times for all 22 samples were less than 4 seconds. This metric passes. All stents were successfully deployed per the IFU.

No overlap or chronic long-length stenting was performed in pre-clinical animal studies due to limitations associated with vessel length and taper. The safety and effectiveness of all stent sizes, including the long length stents and those deployed in overlapping conditions have been addressed in engineering studies – please refer to Table 3 for summary.

X. SUMMARY OF PRIMARY CLINICAL STUDY

The applicant performed a clinical study to establish a reasonable assurance of the safety and effectiveness of the Supera® Peripheral Stent Systems for improving luminal diameter in the treatment of de novo or restenotic lesion(s) up to 140mm in length in the native superficial femoral artery and/or proximal popliteal arteries with reference vessel diameters ranging from 4-6mm, in the US under IDE G070239. 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**

The applicant conducted a study titled "Comparison of the SUpera® PERipheral System to a Performance Goal Derived From Balloon Angioplasty Clinical Trials in the Superficial Femoral Artery" (SUPERB). SUPERB was a prospective, multi-center, non- randomized, un-blinded single arm clinical study comparing percutaneous transluminal angioplasty (PTA) and primary stenting with the Supera® Peripheral Stent Systems to performance goals of PTA alone in the treatment of atherosclerotic lesions of the native superficial femoral artery (SFA) or the superficial femoral and proximal popliteal arteries. The safety performance goal was derived from literature and the effectiveness performance goal was based on an aggregate of published trial data as described by VIVA Physicians Inc. (VPI). There were a total of 49 participating sites in the US; 46 of these sites enrolled 325 roll-in and intent-to treat (ITT) subjects, with ITT subjects defined as the subjects to be included in the statistical analyses of study endpoints. Of these 46 sites, 34 enrolled 264 ITT subjects into the study. Eligible subjects either had stenotic, restenotic (non-stented) or occluded lesions. The reference vessel diameter of the treated subjects was to be 4.0 - 6.0 mm and the lesion length from 4-14 cm. Subjects with Rutherford/Becker Clinical Categories of 2-4 were included in the study. Subject follow-up occurred at 30 days, 6 months, 12 months, and 24 months, and will continue with annual follow-up for up to 3 years.

Patients were treated between July 30, 2009 and May 20, 2011. The database for this PMA reflected data collected through November 1, 2013, and included the 264 ITT patients. There were 46 investigational sites that enrolled subjects.

The primary study endpoints were as follows:

- The primary safety endpoint for the SUPERB SFA/PPA study was a composite of Major Adverse Events (MAEs) defined as all death, TLR or any amputation of the index limb to 30 days (±7 days).
- The primary effectiveness endpoint for the SUPERB SFA/PPA study was primary stent patency rate at 12 months. Primary patency was defined as Peak Systolic Velocity (PSV) ratio < 2.0 at the stented target lesion assessed by duplex ultrasound (DUS) with no clinically-driven reintervention within the stented segment.

Study success was declared only if both primary endpoints (safety and effectiveness) met their performance goals. For the primary safety endpoint, the null hypothesis was rejected if the lower limit on the one-sided 95% confidence interval calculated using the Wilson Score Method on the 30 day freedom from MAE rate exceeded the performance goal (PG) of 88.0%. For the primary

effectiveness endpoint, the null hypothesis was rejected if the lower limit of the one-sided 95% confidence interval calculated using the Wilson Score Method on the 12 month patency rate exceeded the PG of 66%.

The SUPERB Study was monitored by independent contract monitors. Independent duplex ultrasound and angiographic core laboratories reviewed and analyzed key study variables. An independent Data Safety Monitoring Board (DSMB) was used to review study data on an ongoing basis and identify any potential safety trends. Adjudication of major adverse events was conducted by an independent Clinical Events Committee (CEC).

1. Clinical Inclusion and Exclusion Criteria

Enrollment in the SUPERB SFA/PPA study was limited to patients who met the following inclusion/exclusion criteria (**Table 5**).

Table 5: Inclusion and Exclusion Criteria

Inclusion Criteria	**Exclusion Criteria**
1. Age ≥ 18 years and of age of legal consent.	1. Thrombophlebitis or deep venous thrombus, within the previous 30 days.
2. Women of child bearing potential must have a negative pregnancy test within 7 days prior to the index procedure.	2. Receiving dialysis or immunosuppressant therapy within the previous 30 days.
3. Subject has lifestyle limiting claudication or rest pain (Rutherford-Becker scale 2-4) with a resting ABI ≤ 0.9. Resting TBI is performed only if unable to reliably assess ABI. TBI must be ≤0.7. These assessments are required for the target limb, but both limbs are preferred.	3. Thrombolysis of the target vessel within 72 hours prior to the index procedure, where complete resolution of the thrombus was not achieved. 4. Stroke within the previous 90 days. 5. Ipsilateral femoral aneurysm **or** aneurysm in the SFA or popliteal artery. 6. Required stent placement via a popliteal approach.
4. A single superficial femoral artery lesion with >60% stenosis or total occlusion.	7. Required stent placement across or within 0.5cm of the SFA / PFA bifurcation.
5. Stenotic lesion(s) or occluded length within the same vessel (one long or multiple serial lesions) ≥ 40mm to ≤ 140mm. Reference vessel diameter (RVD) ≥ 4.0mm and ≤ 6.0mm by visual assessment.	8. Procedures which are pre-determined to require stent-in-stent placement to obtain patency, such as in-stent restenosis. 9. Significant vessel tortuosity or other parameters prohibiting access to the lesion or 90° tortuosity which would prevent delivery of the stent device.
6. All lesions are to be located with the distal point at least 3cm above the knee joint, defined as the distal end of the femur at the knee joint, and proximal point at least 2cm below the origin of the profunda artery.	10. Required stent placement within 1cm of a previously deployed stent. 11. Subject required a coronary intervention, and the coronary intervention was done less than 7 days prior to or planned within 30 days after the treatment of the target lesion.
7. Patent infrapopliteal and popliteal	12. Known allergies to any of the following:

Inclusion Criteria	Exclusion Criteria
artery, i.e., single vessel runoff or better with at least one of three vessels patent (<50% stenosis) to the ankle or foot. 8. The target lesion(s) can be successfully crossed with a guide wire and dilated. 9. Poor aortoiliac or common femoral "inflow" (i.e. angiographically defined >50% stenosis of the iliac or common femoral artery) that would be deemed inadequate to support a femoropopliteal bypass graft ***must*** be successfully treated prior to treatment of the target lesion. This can be done just prior to treatment of the target lesion. Successful treatment is defined as <30% stenosis after either PTA or stenting of the inflow lesion. After treatment of the inflow lesion, the residual pressure gradient across the target lesion will be obtained and if the peak to peak pressure gradient is ≤ 20mmHg, the subject will be included in the study. 10. A subject with bilateral obstructive SFA disease is eligible for enrollment into the study. If a subject with bilateral disease is enrolled, the target limb will be selected at the Investigator's discretion, who may use the criteria of lesion length, percent stenosis, and/or calcification content. The contra-lateral procedure should not be done until at least 30 days after the index procedure (staged); however, if contra-lateral treatment is performed prior to treatment of the target lesion, the waiting period will be at least 14 days prior to the index procedure. 11. The subject is eligible for standard surgical repair, if necessary. 12. A subject who requires a coronary intervention should have it performed at least 7 days prior to the treatment of the target lesion. 13. Subject must provide written informed consent. 14. Subject must be willing to comply with the specified follow-up evaluation schedule.	aspirin **and all three of the following:** clopidogrel bisulfate (Plavix®), ticlopidine (Ticlid ®),**and** prasugrel (Effient®); heparin; Nitinol (nickel titanium); or contrast agent, that cannot be medically managed. 13. Presence of thrombus prior to crossing the lesion. 14. Known or suspected active infection at the time of the procedure. 15. Presence of an ipsilateral arterial artificial graft. 16. Use of cryoplasty, laser, or atherectomy devices in the target vessel at the time of index procedure. 17. Restenotic lesion that had previously been treated by atherectomy, laser or cryoplasty within 3 months of the index procedure. 18. Subject has tissue loss, defined as Rutherford-Becker classification category 5 or 6. 19. History of neutropenia, coagulopathy, or thrombocytopenia that was unexplained or is considered to be at risk for reoccurance. 20. Known bleeding or hypercoagulability disorder or significant anemia (Hb<8.0) that cannot be corrected. 21. Subject has the following laboratory values: a. platelet count less than 80,000/μL, b. international normalized ratio (INR) greater than 1.5, c. serum creatinine level greater than 2.0 mg/dL. 22. Subject requires general anesthesia for the procedure. 23. Subject is pregnant or plans to become pregnant during the study. 24. Subject has a co-morbid illness that may result in a life expectancy of less than 1 year. 25. Subject is participating in an investigational study of a new drug, biologic or device at the time of study screening. NOTE: Subjects who are participating in the long term follow-up phase of a previously investigational and now FDA-approved product are not excluded by this criterion.

2. Follow-up Schedule

All patients were scheduled to return for follow-up evaluations at 30 days, 6 months, 1, 2, and 3 years post-procedure. **Table 6** provides a summary of the specific study requirements at each stage of the study.

Table 6: Study Assessment Schedule and Requirements

TESTING	Baseline[1]	Implant Procedure	Discharge	Month 1 (±7 days)	Month 6 (±14 days)	Month 12 (±30 days)	Month 24 (±30 days)	Month 36 (±30 days)	Unscheduled Visit
Informed Consent/HIPAA	X								
Inclusion/Exclusion Criteria	X								
Demographics and Medical History	X								
Brief Physical Exam/ Health Status[2]	X		X	X	X	X	X	X	
Routine Laboratory Tests including CBC, platelet count, serum creatinine, INR, pregnancy test	X		X						
CK/CK-MB enzymes			X[3]						
ECG	X		X	X[4]					
Angiography		X[5]							X
Device Accountability		X							
Duplex ultrasound			X[6]		X	X	X	X	X
Rutherford-Becker Scales[7]	X			X	X	X	X	X	X
ABI and TBI[8]	X			X	X	X			X
Anti-platelet/anti-coagulation medication[9]	X	X	X	X					
Quality of Life Questionnaires	X				X	X			
Exercise Tolerance Testing (ETT)	X[10]			X[10]		X[10]			
X-ray of the treated limb						X	X	X	X
Adverse Events	X	X	X	X	X	X[11]			X[11]
Serious Adverse Events (SAE)	X	X	X	X	X	X[11]	X[11]	X[11]	X[11]
Unanticipated Adverse Device Effects (UADE)		X	X	X	X	X[11]	X[11]	X[11]	X[11]
Protocol Deviations	X	X	X	X	X	X	X	X	X

[1] Baseline (pre-procedure) measurements were obtained within 30 days prior to the index procedure (also refer to footnote 3 of this table). Use of retrospective assessments, prior to signing of informed consent, were used if they were performed as routine standard of care.

[2] Brief physical exam at baseline were targeted to assessment of limb ischemia and concurrent medical conditions to assess subject eligibility for study participation. Health status assessment was performed at discharge and subsequent clinic visits to assess for limb ischemia and other changes in medical conditions that were reportable as adverse events.

[3] CK at discharge time point was obtained only if subject showed signs or symptoms of cardiac ischemia. CK-MB was required if CK was elevated (≥ 2X the laboratory upper limit of normal). If CK and CK-MB were elevated, then acute myocardial infarction was diagnosed, and subject would be treated according to hospital procedures.

[4] 30 day ECG performed if subject experienced any ischemic cardiac symptoms since discharge.

[5] Angiography performed both pre- and post-procedure to record data needed for percent diameter stenosis and other measures. Additional angiography was performed at Investigator discretion or to assess events.

[6] Duplex ultrasound was completed within 37 days post-procedure. Duplex ultrasound at 24- or 36-month was not required unless indicated to rule out limb ischemia/restenosis in subject with suggestive clinical signs or symptoms.

[7] At baseline Clinical Category Scale, during the follow-up both Clinical Category and Clinical Improvement Rutherford-Becker Scales.

[8] Performed Toe Brachial Index (TBI) only if unable to reliably assess ABI reading. Tests were performed in resting state. Post-procedure follow up assessments depended upon which test was performed pre-procedure.

[9] Plavix® or Ticlid® was recommended for at least one month post procedure; ASA recommended for all subjects indefinitely. If Ticlid® was used, subject should have CBC with differential drawn every two weeks for the duration of therapy.

[10] 100 non-roll-in subjects only. Performed post-procedure only if baseline ETT was performed.

[11] All Adverse Events (inclusive of SAEs and UADEs) were to be collected through 12 months post-procedure. After the 12 month (primary endpoint) clinical visit, only SAE/UADE were required to be reported. Data related to pre-existing adverse events (reported through the 12 month visit) were attempted to be reconciled and resolved.

3. Clinical Endpoints

With regard to success/failure criteria, the SUPERB SFA/PPA study was designed to compare the primary clinical endpoints to pre-established performance goals of 88% for safety and 66% for effectiveness (as defined below).

The **primary safety endpoint** was a composite of all death, Target Lesion Revascularization (TLR), or any amputation of the index limb to 30 (±7) days.

Secondary safety endpoints included:

- The combined rate of death at 30 (±7) days, target lesion revascularization (TLR), index limb amputation, and an increase in Rutherford-Becker Classification by 2 classes (comparing pre- to post-procedural assessments) at 12 months.
- Major adverse vascular event (MAVE) at 30 days, 6 months (180 ± 14 days) and 12 months (360 ± 30 days) defined as stent thrombosis, target limb amputation, clinically apparent distal embolization, defined as causing end-organ damage(e.g. lower extremity ulceration, tissue necrosis, or gangrene), procedure related arterial rupture, acute limb ischemia, or bleeding event requiring transfusion.
- Stent integrity assessed by x-ray evaluation at 1, 2, and 3 year follow-up.

The **primary effectiveness endpoint** was the SFA/PPA primary patency rate at 12 months (360 ± 30 days), defined as freedom from restenosis [diameter

stenosis >50% with a peak systolic velocity (PSV) ratio ≥ 2.0 as measured by duplex ultrasound] and TLR.

Secondary effectiveness endpoints included:

- Acute technical (lesion) success, procedural success and device success
- Ankle-Brachial Index (ABI) and Toe-Brachial Index (TBI) at 1, 6 and 12 months
- Target vessel revascularization (TVR) at 6 and 12 months
- Limb ischemia by Rutherford-Becker Classification at Baseline, 1, 6, and 12 months.
- Number of any type of index limb amputations at 6 and 12 months
- Quality of Life as assessed by disease-specific questionnaires at baseline, 6 and 12 months.
- Absolute Claudication Distance as measured by the Exercise Tolerance Test (TASCII) assessed in 100 subjects at baseline, 30 days, and 12 months.
- SFA patency at 6 months using a PSVR ≤ 2.0, and at 6 and 12 months using a PSVR > 2.4
- Target lesion revascularization (TLR) at 6 and12 months

Additional Planned Analyses:

A combined rate of death at 30 days, or TLR, index limb amputation, and an increase in Rutherford-Becker Classification by 2 classes (comparing pre- to post-procedural assessments) measured at 24 and 36 months.

Target vessel revascularization (TVR) at 24 and 36 months post-procedure.

Limb ischemia improvement by Rutherford-Becker (improvement in scale by ≥ 1) at 24 and 36 months.

Major Adverse Vascular Event (MAVE) by 6, 12, 24 and 36 months, defined as:

- stent thrombosis, target limb amputation, or clinically apparent distal embolization, defined as causing end-organ damage (e.g. lower extremity ulceration, tissue necrosis, or gangrene).
- procedure related arterial rupture, acute limb ischemia, or bleeding event requiring transfusion.

Number of any type of index limb amputations at 12, 24 and 36 month follow-up.

Target lesion revascularization (TLR) at 24 and 36 months post-procedure.

B. Accountability of PMA Cohort

A total of 61 roll-in patients signed the informed consent and were enrolled. After the roll-in phase of the study was completed, a total of 264 patients signed the

informed consent and were enrolled in the SUPERB trial. These 264 patients comprised the intent-to-treat (ITT) population.

At the time of database lock, of the 264 ITT patients enrolled in PMA study, 89.4% (n = 236) of patients were evaluable (had follow up > 330 days or had an event) for analysis at the 12-month endpoint and the 24-month post-operative visit.

Table 7 summarizes the study compliance for all follow-up time points.

Table 7: Summary of Subject Follow-up Visit Compliance – ITT Population

Subject Compliance	N=264 Subjects
30-day Follow-up	
Eligible Subjects[a]	260
Follow-up Visit Completed	259
Follow-up Compliance[b] (%)	99.6
6-Month Follow-up	
Eligible Subjects[a]	244
Follow-up Visit Completed	235
Follow-up Compliance[b] (%)	96.3
12-Month Follow-up	
Eligible Subjects[a]	234[c]
Follow-up Visit Completed	232
Follow-up Compliance[b] (%)	99.2
24-Month Follow-up	
Eligible Subjects[a]	206
Follow-up Visit Completed	203
Follow-up Compliance[b] (%)	98.5
36-Month Follow-up[c]	
Eligible Subjects[a]	95
Follow-up Visit Completed	94
Follow-up Compliance[b] (%)	98.95

[a]Eligible subjects are all subjects who were enrolled and have not died, been lost to follow-up, withdrawn, had no information available or declined follow-up prior to the visit window at 30 days, 6 months, 12 months or 24 months.

[b]Percentage is based on number of subjects who had a follow-up visit divided by number of eligible subjects.

[c]36=Month follow-up was ongoing at the time of data export.

N = Intent-To-Treat Population

C. Study Population Demographics and Baseline Parameters

The SUPERB SFA/PPA clinical study included 264 subjects with symptomatic ischemic PAD. The Intent-to-Treat population results indicate the mean age for subjects was 69 years, of which 63.6% (168/264) were male and 43.5% (114/262) had diabetes mellitus, and 66.9% (176/263) had a history of coronary artery

disease. The demographics of the study population are typical for an interventional peripheral vascular study performed in the US. Baseline demographic and clinical characteristics for all subjects enrolled in the SUPERB study are summarized in **Table 8**.

Table 8: Demographics and Baseline Clinical Characteristics – ITT Population

Patient Characteristics	ITT Population (N=264 Patients)
Age[1] (year)	
Mean±SD (N)	68.7±10.0 (264)
Median	70.0
Range (Min, Max)	(40.0,93.0)
Sex	
Male	63.6% (168/264)
Risk Factors	
Hypertension	93.9% (248/264)
Dyslipidemia	86.7% (229/264)
Diabetes Mellitus	43.5% (114/262)
Cigarette Smoking	
Former	48.1% (127/264)
Current	31.8% (84/264)
Renal Insufficiency	9.1% (24/264)
Medical History	
Coronary Artery Disease	66.9% (176/263)
Previous Peripheral Artery Revascularization or Surgery	38.0% (100/263)
Previous Percutaneous Coronary Revascularization	36.1% (95/263)
Coronary Artery Bypass Graft Surgery	27.3% (72/264)
Myocardial Infarction	20.3% (52/256)
Cerebrovascular Accident	9.8% (26/264)
Transient Ischemic Attack	6.1% (16/263)
Deep Vein Thrombosis	2.3% (6/264)
Amputation	1.1% (3/264)
Thrombophlebitis	0.4% (1/264)
Thrombocytopenia	0.4% (1/264)
Clinical Characteristics	
Rutherford Becker Scale	
(2) Moderate Claudication	37.5% (99/264)
(3) Severe Claudication	57.2% (151/264)
(4) Ischemic Rest Pain	5.3% (14/264)
Ankle Brachial Index	
Mean±SD (N)	0.73±0.18 (257)
Range (Min, Max)	(0.00,1.71)

[1] Age is calculated by rounding the value of procedure date-birth date.

Table 9 presents baseline lesion characteristics (assessed by the angiographic core laboratory except as otherwise noted), including lesion location, length and pre-procedure vessel diameter. Results for lesion length are consistent with the differences in methodology, with mean lesion length of 82.3 mm reported by the site investigators and 78.1 mm reported by the core laboratory. Per site assessment, normal-to-normal lesion was determined by measuring the length of the target lesion from healthy tissue to healthy tissue. In contrast, 20-to-20 lesion length was determined by the core laboratory, measuring between the proximal and distal points at which the lesion exhibited 20% stenosis. The mean percent diameter stenosis was 78.0% and the lesion distribution included 24.6% completely occluded lesions and 44.7% severely calcified lesions.

Table 9: Baseline Target Lesion Characteristics – ITT Population

Lesion Characteristics	**N of patients=264 N of segments=265**
SFA Location	
Proximal SFA	12.1% (32/265)
Middle SFA	54.3% (144/265)
Distal SFA	31.7% (84/265)
Distal SFA extending into Popliteal[1]	10.9% (29/265)
Popliteal, above knee	1.9% (5/265)
Lesion length (mm) (Normal-to-normal) [2]	
Mean±SD (N)	82.8±33.0 (273)
Range (Min,Max)	(20.0,140.0)
Lesion length (mm) (20-to-20) [3]	
Mean±SD (N)	78.1±42.78 (264)
Range (Min,Max)	(8.51,236.40)
Pre-procedure Reference Vessel Diameter (mm)	
Mean±SD (N)	4.96±0.92 (265)
Range (Min,Max)	(2.71,7.52)
Pre-procedure Minimum Lumen Diameter (mm)	
Mean±SD (N)	1.1±0.88 (265)
Range (Min,Max)	(0.00,3.52)
Pre-procedure Diameter Stenosis (%)	
Mean±SD (N)	78.0±16.76 (265)
Range (Min,Max)	(42.84,100.00)
Target Lesions treated with 1 study stent[4]	95.8% (251/262)
Target Lesions treated with 2 study stents[4]	3.8% (10/262)
Target Lesions treated with 3 study stents[4]	0.4% (1/262)

Lesion Characteristics	N of patients=264 N of segments=265
Total Occlusion	24.6% (65/264)
Bend	
> 45-89 degrees	0.0% (0/265)
> 90 degrees	0.0% (0/265)
Thrombus	0.0% (0/265)
Eccentric	41.1% (109/265)
Calcification	
Mild	27.3% (72/264)
Moderate	28.0% (74/264)
Severe	44.7% (118/264)
Ulceration Present	15.5% (41/265)
Aneurysm Present	0.8% (2/265)
TASC II Lesion Type	
A	55.5% (147/265)
B	38.9% (103/265)
C	5.7% (15/265)

[1] Subset of SFA lesions based upon Core Lab's further analysis of the data.
[2] *Normal-to-normal* lesion length assessed per site investigator.
[3] Core lab assessed.
[4] Site Reported.

The total number of subjects who withdrew from the study, were lost to follow-up, or died, regardless of the follow-up visit or visit-window status through the duration of the study are provided in **Table 10.**

Table 10: Subjects who have exited the study at any time point as of November 1, 2013 (ITT Population)

Exited Study	Subjects
Died	21/264 (7.95%)
Lost-to-Follow-Up (LTFU)	21/264 (7.95%)
Withdrew	21/264 (7.95%)
Total	63/264 (23.9%)

D. Safety and Effectiveness Results

1. Safety Endpoints

The primary analysis of safety was based on the 264 ITT subjects. The key safety outcomes for this study are presented in **Tables 11 to 13** below. Adverse effects are reported in **Table 12.**

The primary safety endpoint (the composite rate of freedom from all death, target lesion revascularization or any amputation of the index limb to 30 days (±7 days) following stent implantation) was compared to a pre-determined

safety goal of 88%. Of the enrolled ITT subjects with the 30-day (±7 days) evaluable data (n=260), 99.2% (258/260) met the primary safety endpoint (one-sided lower 95% Wilson Score CL of 97.7%) demonstrating statistical significance (p<0.001) when comparing this rate to the 88% performance goal.

Table 11: Summary of Primary Safety Endpoints (30 ± 7 days)

N=264
Lesions = 265

Primary Safety Endpoint	% (num/denom)	Performance Goal	Lower Bound of 95% one-sided Wilson CL	Lower Bound of 97.5% one-sided Wilson CL	Objective Met
Freedom from Death, Target Lesion Revascularization (TLR) or any amputation of the index limb	99.2% (258/260)	88.0%	97.7%*	97.2%	Yes
Freedom from All Cause Death	99.6% (259/260)				
Freedom from TLR	99.6% (259/260)				
Freedom from Amputation of the index limb	100.0% (260/260)				

Note:
Subjects are included in the clinical endpoint evaluation if:

1. They return for their corresponding visit within the window OR
2. They came back for a later scheduled or un-scheduled visit (i.e. a visit form is filled and the sponsor has documented information about their clinical status within the endpoint time frame) OR
3. The last contact date predated the endpoint time frame (they withdrew, were LTFU, died or exited the study for other reasons) BUT had an endpoint event within the endpoint time frame.

Specifically, events defined for the period of 30 days post-procedure follow up are reported for subjects with at least 37 days of follow-up or had 30-day visit within window (30±7 days) or with event to 37 days
*The p-value comparing the rate to the performance goal is < 0.001 using a one-sided binomial exact method.

Additional primary safety analyses were performed, to handle the issue of missing data. In the worst-case scenario, where four subjects with missing primary safety endpoints were considered failures, the rate of freedom from death, TLR or any amputation of the index limb was 97.7% with a one-sided 95% Wilson Score CL of 95.7%, which was still higher than the performance goal of 88%.

Adverse Effects That Occurred in the PMA Clinical Study

There have been twenty two (22) subject deaths reported for the ITT population in this study. Twenty-one (21) subject deaths have been adjudicated by the Clinical Events Committee (CEC) and are unrelated to the Supera®

stent. One subject died on day 1183 which is outside of the 36 month follow-up window.

Table 12 presents a summary of cumulative adverse events documented in the study and includes events with at least one occurrence to 24 months.

Table 12: Summary of Adverse Events Cumulative to Time-Point – ITT Population

System Organ Class/Preferred Term	Events at ≤ 1 month	Events at ≤ 12 months	Events at ≤ 24 months
Any AE	43.1% (110/255)	79.8% (198/248)	84.9% (203/239)
Blood and lymphatic system disorders	2.7% (7/255)	5.6% (14/248)	7.1% (17/239)
Cardiac disorders	3.5% (9/255)	20.6% (51/248)	24.7% (59/239)
Congenital, familial and genetic disorders	NA	0.4% (1/248)	0.8% (2/239)
Ear and labyrinth disorders	NA	0.4% (1/248)	0.4% (1/239)
Endocrine disorders	NA	0.4% (1/248)	0.8% (2/239)
Eye disorders	NA	0.8% (2/248)	0.8% (2/239)
Gastrointestinal disorders	3.1% (8/255)	11.3% (28/248)	14.6% (35/239)
General disorders and administration site conditions	16.5% (42/255)	27.0% (67/248)	31.0% (74/239)
Hepatobiliary disorders	NA	0.4% (1/248)	0.8% (2/239)
Immune system disorders	0.4% (1/255)	0.8% (2/248)	0.8% (2/239)
Infections and infestations	3.1% (8/255)	10.5% (26/248)	12.1% (29/239)
Injury, poisoning and procedural complications	2.4% (6/255)	15.7% (39/248)	19.2% (46/239)
Investigations	NA	2.0% (5/248)	2.1% (5/239)
Metabolism and nutrition disorders	0.8% (2/255)	3.6% (9/248)	5.0% (12/239)
Musculoskeletal and connective tissue disorders	10.6% (27/255)	24.2% (60/248)	27.2% (65/239)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	0.4% (1/255)	2.0% (5/248)	2.9% (7/239)
Nervous system disorders	2.7% (7/255)	10.9% (27/248)	12.1% (29/239)
Psychiatric disorders	0.4% (1/255)	2.0% (5/248)	2.5% (6/239)
Renal and urinary disorders	1.6% (4/255)	4.0% (10/248)	5.4% (13/239)
Reproductive system and breast disorders	0.4% (1/255)	0.8% (2/248)	0.8% (2/239)
Respiratory, thoracic and mediastinal disorders	1.2% (3/255)	9.3% (23/248)	13.0% (31/239)
Skin and subcutaneous tissue disorders	1.6% (4/255)	4.4% (11/248)	5.4% (13/239)
Surgical and medical procedures	NA	1.2% (3/248)	1.7% (4/239)
Vascular disorders	18.8% (48/255)	39.5% (98/248)	46.0% (110/239)

Note:

Subjects included in each interval are as follows:

≤ 1 month: subjects who had SAE occurring between 0 – 37 days post procedure or with follow up time for AE ≥ 37 days.

≤ 12 months: subjects who had SAE occurring between 0 - 390 days post procedure or with follow up time for AE ≥ 390 days.

≤ 24 months: subjects who had SAE occurring between 0 - 750 days post procedure or with follow up time for AE ≥ 750 days.

Secondary Endpoint Safety Analysis

Table 13: Summary of Secondary Safety Endpoints

Secondary Safety Endpoints	ITT Population (264 Subjects, 265 Segments)
Stent Fracture - At 12 Months	0.0% (0/228)
Stent Fracture – At 24 Months*	0.5% (1/200)
Major Adverse Vascular Event (MAVE) at 30 days	1.2% (3/260)
Major Adverse Vascular Event (MAVE) at 6 Months	2.5% (6/241)
Major Adverse Vascular Event (MAVE) at 12 Months	3.8% (9/235)
Major Adverse Vascular Event (MAVE) at 24 Months	5.3% (11/207)
Safety Composite Endpoint (Death at 30 days, TLR, Index Limb Amputation and Rutherford-Becker Classification Increase By 2 Classes at 12 Months) [3]	12.45% (29/233)
Death At 30 Days	0.4% (1/260)
TLR To 12 Months	11.1% (26/235)
Index Limb Amputation At 12 Months	0.4% (1/233)
Rutherford-Becker Classification Increase By 2 Classes As Compared To Pre-Procedure at 12 Months	1.3% (3/230)
Index Limb Amputation at 6 months	0.0% (0/240)
Index Limb Amputation at 12 months	0.4% (1/233)
Index Limb Amputation at 24 months	1.0% (2/205)

Note:

Subjects in the ITT Population are included in the clinical endpoint if:

1. They return for their corresponding visit within the window OR
2. They came back for a later scheduled or un-scheduled visit (i.e. a visit form is completed and the sponsor has documented information about their clinical status within the endpoint time frame) OR
3. The last contact date predated the endpoint time frame (they withdrew, were LTFU, died or exited the study for other reasons) BUT had an endpoint event within the endpoint time frame.

Events defined for the period of 12 months post-procedure follow up are reported for subjects with at least 390 days of follow-up or had 12-month visit within window (360 ± 30 days) or with event to 390 days.

Events defined for the period of 24 months post-procedure follow up are reported for subjects with at least 750 days of follow-up or had 24-month visit within window (720 ± 30 days) or with event to 750 days.

* One subject experienced a Type III fracture at 24 months after three directional atherectomy procedures to treat in-stent restenosis.

Stent Fracture Analysis

As indicated in **Table 14** below, one subject (1/200, 0.5%) experienced a Type III fracture 24 months. The subject had a revascularization with directional atherectomy for in-stent restenosis at 9 month post index procedure. At 12 months follow up there was no evidence of a stent fracture. Additional in-stent restenoses were treated with directional atherectomy between the 12 and 24 month evaluations. At 24 months, a type III fracture was noted by x-ray in the region of the earlier restenoses. There was no report of a major adverse event at 24 months.

Table 14: Stent Fractures at 12-and 24-Months

Stent Fractures[1]	12-Months (N = 243)	24-Months (N=200)
Type I – Single time fracture	0.0% (0/243)	0.0% (0/200)
Type II – Multiple time fractures	0.0% (0/243)	0.0% (0/200)
Type III – Stent fracture(s) with preserved alignment of the components	0.0% (0/243)	0.5% (1/200)
Type IV – Stent fracture(s) with mal-alignment of the components	0.0% (0/243)	0.0% (0/200)
Type V – Stent fracture(s) in a trans-axial spiral	0.0% (0/243)	0.0% (0/200)

[1] Evaluated by X-ray [anterior-posterior (AP) and lateral views in both straight and flexed knee positions] per an independent core lab.

2. Effectiveness Endpoints

The analysis of primary effectiveness was based on 228 evaluable subjects at the 12-month time point, as shown in **Table 15** below.

The primary effectiveness endpoint (primary patency of the stent at 12 months (360 ± 30 days)) was defined as freedom from restenosis [diameter stenosis >50% with a peak systolic velocity (PSV) ratio ≥ 2.0 as measured by duplex ultrasound] and TLR. Of the evaluable subjects, 78.9% (180/228) met the primary effectiveness endpoint (one-sided lower 95% Wilson Score CL of 74.2%), demonstrating statistical significance ($p<0.001$) when comparing this patency rate to the 66% performance goal.

In further consideration of the overall device performance as well as to allow the application of a more modem study design, a secondary analysis of the data was also performed. This was not a pre-specified endpoint and was used for information purposes only. The secondary analysis applied a modified VIVA effectiveness criterion which uses a higher PSV ratio. Using these modified criteria of a PSV ratio < 2.4, the mean primary patency rate as a measure of primary effectiveness at 12 months was 80.3% with a one-sided lower 95% Wilson Score CL of 75.6% and one-sided lower 97.5% Wilson Score CL of 74.6%.

Additionally, 86.7% (196/226) of the subjects had no restenosis (defined as ≥ 50% diameter stenosis) at 12 months and 88.9% (209/235) of the subjects had freedom from Target Lesion Revascularization (TLR) to 12 months. At 24 months (720±30 days), 84.3% (177/213) of the subjects had freedom from TLR.

Table 15: Summary of Primary Effectiveness Endpoints

Primary Effectiveness Endpoint (PSVR < 2.0)	Primary Stent Patency Rate	Performance Goal	Lower Bound of 95.0% one-sided Wilson CL	Lower Bound of 97.5% one-sided Wilson CL	Objective Met
Patency rate at 12 months	78.9% (180/228)[1]	66.0%	74.2%*	73.2%	Yes
No Restenosis at 12 months**	86.7% (196/226)[2]				
Freedom from TLR at 12 months***	88.9% (209/235)[3]				

Note:

Subjects in the ITT Population are included in the clinical endpoint evaluation if:

1. They return for their corresponding visit within the window OR
2. They came back for a later scheduled or un-scheduled visit (i.e. a visit form is filled and the sponsor has documented information about their clinical status within the endpoint time frame) OR
3. The last contact date predated the endpoint time frame (they withdrew, were LTFU, died or exited the study for other reasons) BUT had an endpoint event within the endpoint time frame.

Specifically, events defined for the period of 12 months post-procedure follow up are reported for subjects with at least 390 days of follow-up or had 12-month visit within window (360±30 days) or with event to 390 days.

Subjects are included in the denominator for the image (restenosis) endpoint time frame if:

1. They returned for corresponding visit within the pre-specified visit window, e.g. 360 ± 30 days for the 12 Month Restenosis endpoint.
2. They came back for an earlier or later scheduled or unscheduled visit that is after the corresponding visit window and the subject's vessel is patent and an earlier imaging visit shows the vessel is patent OR the subject's vessel is not patent and an earlier imaging visit shows the vessel is not patent

Patency is PSVR < 2.0; Restenosis is PSVR ≥ 2.0

*The p-value comparing the rate to the performance goal is < 0.001 using a one-sided binomial exact test.

**No stenosis ≥50% diameter stenosis.

***One subject had a TVR, during which a balloon was inflated in the proximal segmental study stent. At that time the study stent was patent. Thus the TLR was non-clinically driven. This subject was censored from the primary patency analysis.

[1]234 subjects eligible – 2 missed visit – 7 other missing data + 1 patent at subsequent DUS + 2 revascularized prior to assessment.

[2]234 subjects eligible – 2 missed visit – 7 other missing data + 1 patent at subsequent DUS.

[3]235 subjects eligible for freedom from TLR (includes the patient mentioned above with the non-clinically driven TVR)

A missing data analysis was performed on the primary effectiveness endpoint. In the most conservative case where the ITT subjects with missing primary effectiveness endpoints were considered not patent (the worst-case scenario), the patency rate at 12 months is 68.2% (180/264) with the one-sided 95% lower confidence limit of 63.3%. Based on the tipping point analysis, eight out of 36 patients (22.2%) with missing primary effectiveness endpoint data would need to be patent to meet the objective. This outcome is likely considering that the observed rate was 78.9%. In addition, a multiple imputation was performed where missing 12-month patency data was imputed to show the robustness of the observed data. The results between the available cases and the imputed cases were similar (78.9% vs. 79.5% respectively); and the one-sided lower 95% confidence limit for both analyses were greater than the performance goal of 66%. This is presented in **Table 16**.

Table 16. Analysis of Primary Efficacy Endpoints -- Missing Data Analysis

Patency Rate At 12 Months (390 Days)	SUPERA Device	Lower Bound Of 95% One-Sided Wilson CL	Performance Goal
Intent-To-Treat Population			
Available Cases*	78.9% (180/228)[1]	74.2%	66%
Available And Imputed Cases - Multiple Imputation**	79.5%	74.8%	66%

* For the available cases:

Subjects in the ITT Population are included in the clinical endpoint evaluation if:

1. They return for their corresponding visit within the window OR
2. They came back for a later scheduled or un-scheduled visit (i.e. a visit form is completed and the sponsor has documented information about their clinical status within the endpoint time frame) OR
3. The last contact date predated the endpoint time frame (they withdrew, were LTFU, died or exited the study for other reasons) BUT had an endpoint event within the endpoint time frame.

Events defined for the period of 12 months post-procedure follow up are reported for subjects with at least 390 days of follow-up or had 12-month visit within window (360±30 days) or with event to 390 days.

Subjects are included in the denominator for the image (restenosis) endpoint time frame if:

1. They returned for corresponding visit within the pre-specified visit window, e.g. 390 ±30 days for the 12 Month Restenosis endpoint
2. They came back for an earlier or later scheduled or unscheduled visit that is after the corresponding visit window and the subject's vessel is patent and an earlier imaging visit shows the vessel is subject OR the subject's vessel is not patent and an earlier imaging visit shows the vessel is not patent

[1]For explanation of denominator, see footnote in Table 15.

**Five data sets were imputed using multiple imputation approach by SAS PROC MI. The covariates used for imputation model were age, sex, diabetes, target lesion length and reference vessel diameter. Means were taken for subjects with multiple lesions. Missing information on these covariates was imputed by mean and median for continuous and categorical variables, respectively. A 95% one-sided CI by Wilson method was obtained by using SAS PROC MIANALYZE on the results of the five significance tests.

Table 17: Primary Patency with a PSVR of ≤ 2.4

Primary Effectiveness Endpoint (PSVR ≤ 2.4)	Primary Stent Patency Rate	Lower Bound of 95% one-sided Wilson CL	Lower Bound of 97.5% one-sided Wilson CL
Patency rate at 12 months	80.3% (183/228)	75.6%	74.6%
No Restenosis at 12 months*	88.1% (199/226)		
Freedom from TLR at 12 months**	88.9% (209/235)***		

Note:

Subjects in the ITT Population are included in the clinical endpoint evaluation if:

1. They return for their corresponding visit within the window OR
2. They came back for a later scheduled or un-scheduled visit (i.e. a visit form is completed and the sponsor has documented information about their clinical status within the endpoint time frame) OR
3. The last contact date predated the endpoint time frame (they withdrew, were LTFU, died or exited the study for other reasons) BUT had an endpoint event within the endpoint time frame.

Specifically, events defined for the period of 12 months post-procedure follow up are reported for subjects with at least 390 days of follow-up or had 12-month visit within window (360±30 days) or with event to 390 days.

Subjects are included in the denominator for the image (restenosis) endpoint time frame if:

1. They returned for corresponding visit within the pre-specified visit window, e.g. 360 ± 30 days for the 12 Month Restenosis endpoint
2. They came back for an earlier or later scheduled or unscheduled visit that is after the corresponding visit window and the subject's vessel is patent and an earlier imaging visit shows the vessel is patent OR the subject's vessel is not patent and an earlier imaging visit shows the vessel is not patent

Patency is PSVR ≤ 2.4; Restenosis is PSVR > 2.4

*No stenosis ≥ 50% diameter stenosis.

**One subject had a TVR, during which a balloon was inflated in the proximal segmental study stent. At that time the study stent was patent. Thus the TLR was non-clinically driven. This subject was censored from the primary patency analysis.

***235 subjects eligible for freedom from TLR.

For explanations of patency and restenosis denominators, see footnotes in Table 15.

Freedom from loss of primary patency at 12 months (360 ± 30 days) (±SE) was achieved in 86.3% (±2.3) of the ITT population (**Figure 4** and **Table 18**). In a secondary analysis of the freedom from loss of patency, in which diameter stenosis >50% was defined with a threshold PSV ratio of >2.4, there was no change in the estimate of freedom from loss of patency in the subjects with DUS performed through 390 days. The primary stent patency rate using survival analysis is presented in **Figure 5**. Freedom from loss of primary patency at 12 months was 80.3%. **Table 19** depicts the probability of freedom from loss of primary patency.

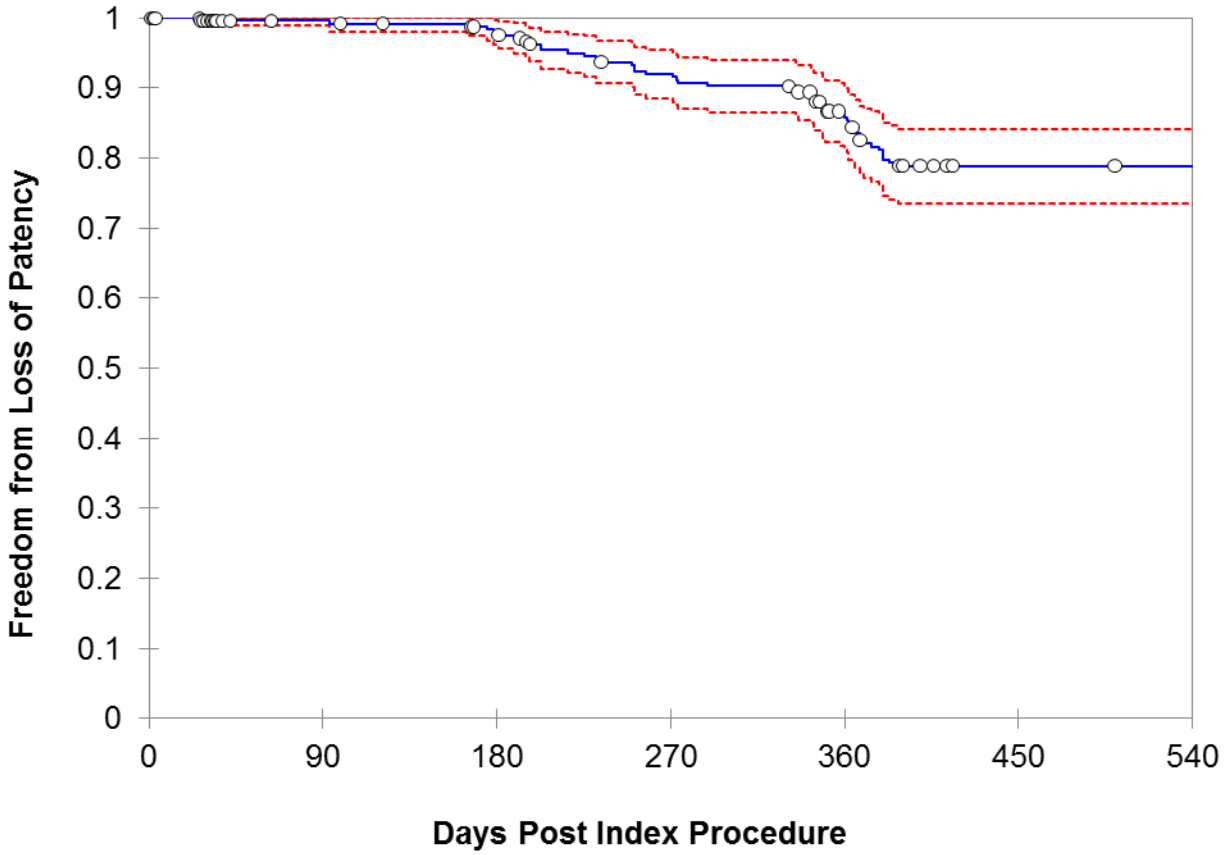


Figure 4: Freedom from Loss of Primary Patency (Restenosis defined as PSV Ratio of ≥ 2.0)

Table 18: Probability of Freedom from Loss of Patency (Restenosis defined as PSV Ratio of ≥ 2.0)

Interval	[0, 90)	[90, 180)	[180, 270)	[270, 360)	[360, 390)	≥391
# At Risk	264	242	234	215	188	169
# Events	1	4	14	13	16	0
# Censored	21	4	5	14**	3**	6
Survival Rate*	1.000	0.996	0.979	0.920	0.863	0.789
Standard Error	0.000	0.004	0.009	0.018	0.023	0.027

Note:
The following set of rules were employed for the Freedom from Loss of Patency analyses:
If a subject is free from TLR or restenosis and their last day of clinical follow-up is< 390 days, the subject is censored at the day after their last clinical follow-up
If a subject has restenosis and a TLR, the event is the day of whichever is earlier
If a subject has no TLR and no DUS at 12 months, they are censored at 331 days
If a subject had no TLR and no DUS at 6 and 12 months, they are censored at 166 days
If a subject had no TLR, restenosis after 390 days and restenosis at an earlier visit, the event is the day of the earlier restenosis
* Survival rate at beginning of time period
** Of the 17 censored patients (14 + 3), only 11 had sufficient follow-up to be included in the primary patency binary endpoint analysis.

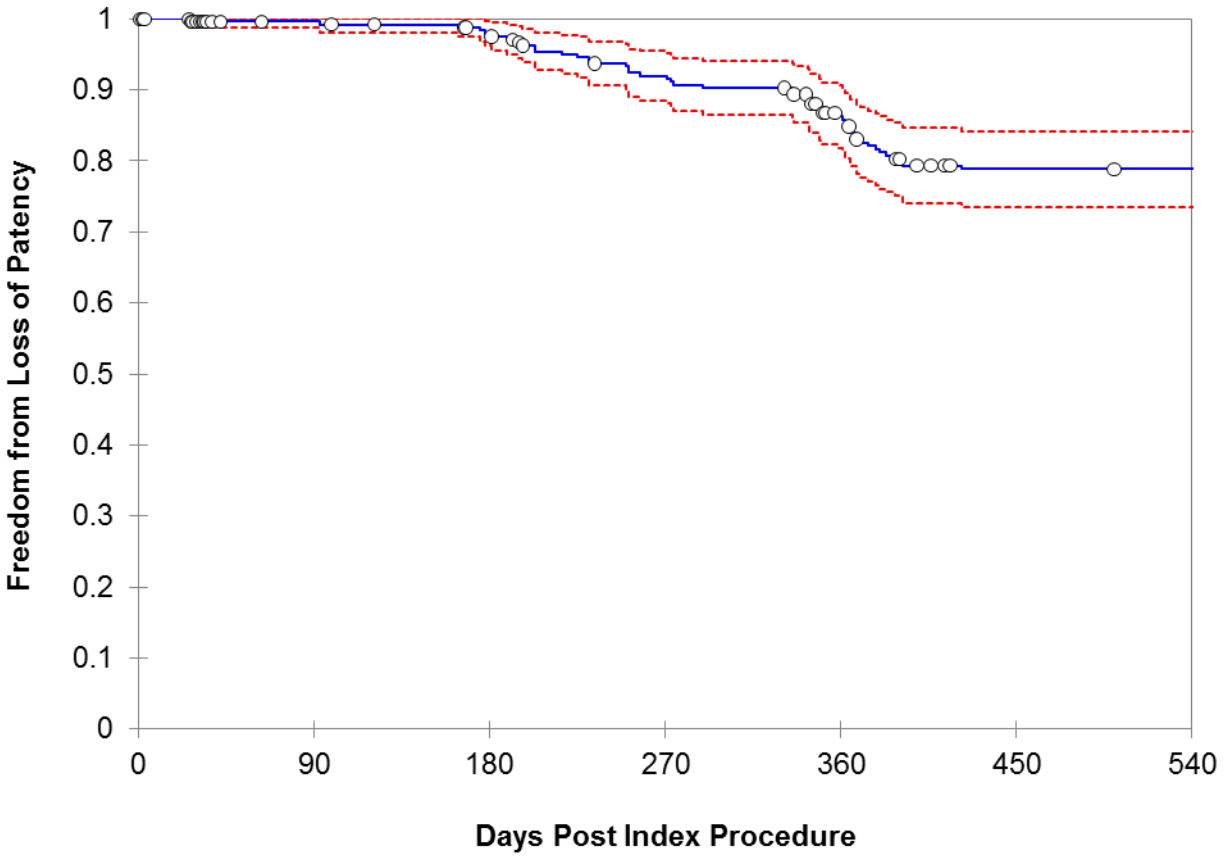


Figure 5: Freedom from Loss of Primary Patency (Restenosis defined as PSV Ratio of > 2.4)

Table 19: Probability of Freedom from Loss of Patency (Restenosis defined as PSV Ratio of > 2.4)

Interval	**[0, 90)**	**[90, 180)**	**[180, 270)**	**[270, 360)**	**[360, 390)**	**≥ 391**
# At Risk	264	242	234	215	188	172
# Events	1	4	14	13	13	3
# Censored	21	4	5	14**	3**	6
Survival Rate*	1.000	0.996	0.979	0.920	0.863	0.803
Standard Error	0.000	0.004	0.009	0.018	0.023	0.026

Note:
The following set of rules were employed for the Freedom from Loss of Patency analyses:
If a subject is free from TLR or restenosis and their last day of clinical follow-up is< 390 days, the subject is censored at the day after their last clinical follow-up
If a subject has restenosis and a TLR, the event is the day of whichever is earlier
If a subject has no TLR and no DUS at 12 months, they are censored at 331 days
If a subject had no TLR and no DUS at 6 and 12 months, they are censored at 166 days
If a subject had no TLR, restenosis after 390 days and restenosis at an earlier visit, the event is the day of the earlier restenosis
* Survival rate at beginning of time period
** Of the 17 censored patients (14 + 3), only 11 had sufficient follow-up to be included in the primary patency binary endpoint analysis.

Freedom from target lesion revascularization at 12 months was achieved in 89.4%% (±2.0%) of the ITT population (**Figure 6** and **Table 20**) and in 84.0% (±2.5%) at 24 months.

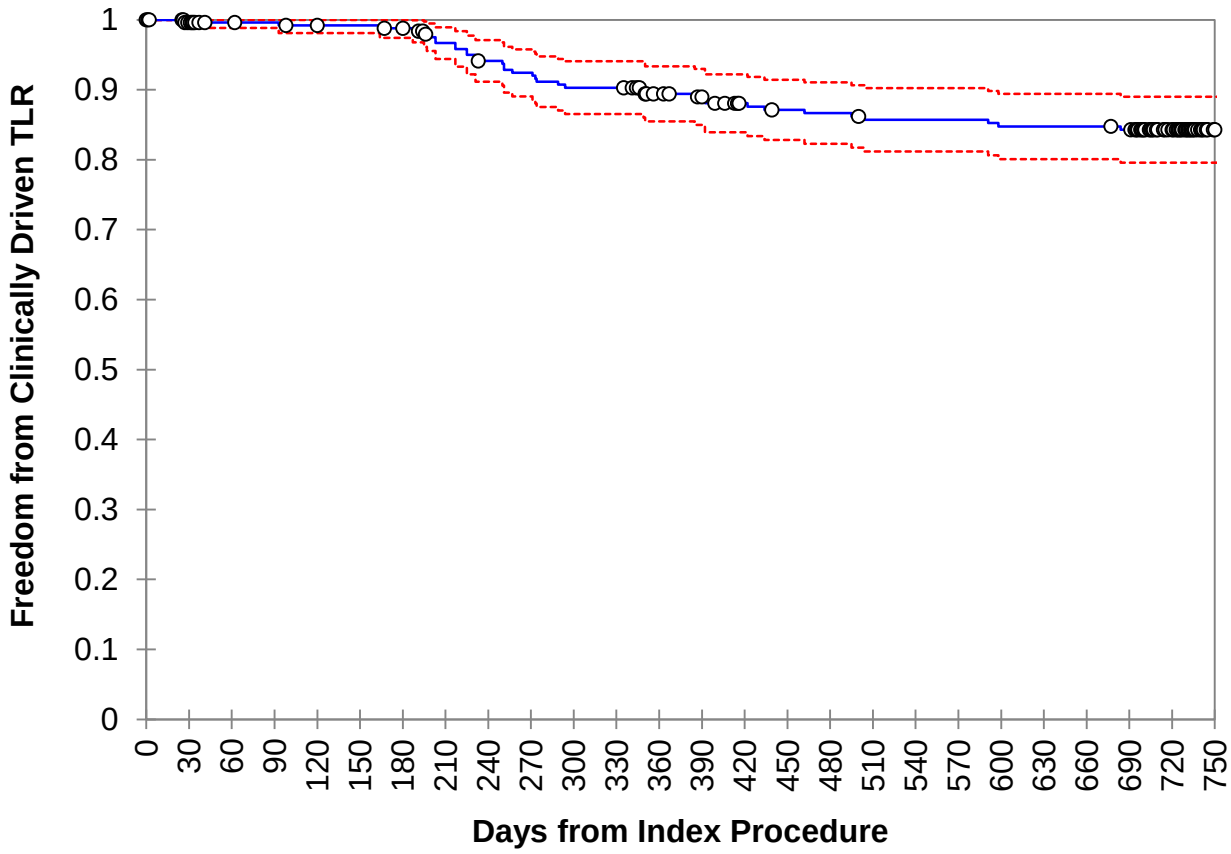


Figure 6. Freedom From Clinically Driven TLR to 24 Months

Table 20: Probability of Freedom from TLR to 24 Months

Interval	**[0, 90)**	**[90, 180)**	**[180, 270)**	**[270, 360)**	**[360, 390)**	**[390, 720)**	**[720,750)**
At risk	264	242	237	217	201	197	149
Failed	1	2	15	7	1	10	0
Censored	21	3	5	9**	3**	38	43
Survival Rate*	1.000	0.996	0.988	0.925	0.894	0.890	0.840
Standard Error	0.000	0.004	0.007	0.017	0.020	0.020	0.025

Note:
The following set of rules were employed for the Freedom from Clinically Driven TLR analyses:
If a subject is free from TLR and their last day of clinical follow-up is< 750 days, the subject is censored at the day after their last clinical follow-up
* Survival rate at beginning of time period
** The 12 censored patients (9 + 3) had sufficient follow-up to be included in the freedom from TLR binary endpoint analysis.

Table 21 presents a lesion length tercile analysis based on SUPERB SFA/PPA Study outcomes and analyzed using a PSV ratio threshold of 2.0 and clinically-driven TLR as well as using modified VIVA criteria using a higher PSV ratio (2.4*)*.

Table 21: Primary Patency at 12 Months as a Function of Lesion Length

	Total N = 262 Total Lesions* = 262 Lesion Length Terciles		
	Lower (N = 87 Subjects N= 87 Lesions)	**Mid (N = 88 Subjects N= 88 Lesions)**	**Upper (N = 87 Subjects N= 87 Lesions)**
Pre-Procedure Lesion Length (mm)			
N	87	88	87
Mean ± SD	35.4±12.3	73.5±10.8	126.1±33.4
Median	36.7	73.4	115.9
Min, Max	(8.5,55.0)	(55.5,91.5)	(91.6,236.4)
Primary Effectiveness Endpoint			
Primary Patency (PSVR < 2.0)Rate at 12 Months**	81.3% (61/75)	78.2% (61/78)	76.7% (56/73)
No Restenosis at 12 months (PSV Ratio $\leq$ 2.0)***	87.7% (64/73)	84.6% (66/78)	87.7% (64/73)
Freedom from TLR to 12 months	92.2% (71/77)	90.2% (74/82)	83.8% (62/74)
Primary Patency (PSVR $\leq$ 2.4)Rate at 12 Months**	85.3% (64/75)	78.2% (61/78)	76.7% (56/73)

	Total N = 262 Total Lesions* = 262 Lesion Length Terciles		
	Lower (N = 87 Subjects N= 87 Lesions)	**Mid (N = 88 Subjects N= 88 Lesions)**	**Upper (N = 87 Subjects N= 87 Lesions)**

Note:
Subjects in the ITT Population are included in the clinical endpoint evaluation if:

1. They return for their corresponding visit within the window OR
2. They came back for a later scheduled or un-scheduled visit (i.e. a visit form is filled and the sponsor has documented information about their clinical status within the endpoint time frame) OR
3. The last contact date predated the endpoint time frame (they withdrew, were LTFU, died or exited the study for other reasons) BUT had an endpoint event within the endpoint time frame.

Subjects are included in the denominator for the image (restenosis) endpoint time frame if:

1. They returned for corresponding visit within the pre-specified visit window, e.g. 360 ± 30 days for the 12 Month Restenosis endpoint
2. They came back for an earlier or later scheduled or unscheduled visit that is after the corresponding visit window and the subject's vessel is patent and an earlier imaging visit shows the vessel is patent OR the subject's vessel is not patent and an earlier imaging visit shows the vessel is not patent

Events defined for the period of 12 months post-procedure follow up are reported for subjects with at least 390 days of follow-up or had 12-month visit within window (360±30 days) or with event to 390 days.

Subjects are included in the denominator for the image (restenosis) endpoint time frame if they returned for corresponding visit within the pre-specified visit window, e.g. 360 ± 30 days for the 12 Month Restenosis endpoint.

One (1) subject had a TVR, during which a balloon was inflated in the proximal segmental study stent. At that time the study stent was patent. Thus the TLR was non-clinically driven. This subject was censored from the primary patency analysis.
N = Intent-To-Treat Population
*Lesions as reported by the Angiographic Core Laboratory. Terciles performed on single lesions: One subject is excluded because of missing lesion length data, and one subject is excluded due to multiple lesions.
**Defined as: uninterrupted patency with no procedures performed on or at the margins of the treated segment, with no restenosis ≥ 50% as documented by DUS peak systolic velocity ratio ≥2.0 or > 2.4
***No stenosis ≥ 50% diameter stenosis.

Note: Site, CEC, Duplex and Angiographic Core Laboratory Reported Table

Table 22: Primary Patency at 12 Months by Core Lab-Assessed Lesion Length

	Total N=262 Total Lesions = 262	
Primary Endpoints	**Lesion length ≤ 140 mm (N=244 Subjects, L=244 Lesions)**	**Lesion length > 140* mm (N=18 Subjects, L=18 Lesions)**
Patency rate at 12 months (PSV Ratio < 2.0)*	80.6% (170/211)	53.3% (8/15)
Kaplan-Meier Estimate	87.9%	55.6%

	Total N=262 Total Lesions = 262	
Primary Endpoints	**Lesion length ≤ 140 mm (N=244 Subjects, L=244 Lesions)**	**Lesion length > 140* mm (N=18 Subjects, L=18 Lesions)**

Note:
Analysis based on the ITT population. Only 262 subjects are included in this analysis. One subject is excluded because of missing lesion length data, and one subject is excluded due to multiple lesions.
Subjects in the ITT Population are included in the clinical endpoint evaluation if:

1. They return for their corresponding visit within the window OR
2. They came back for a later scheduled or un-scheduled visit (i.e. a visit form is filled and the sponsor has documented information about their clinical status within the endpoint time frame) OR
3. The last contact date predated the endpoint time frame (they withdrew, were LTFU, died or exited the study for other reasons) BUT had an endpoint event within the endpoint time frame.

Subjects are included in the denominator for the image (restenosis) endpoint time frame if:

1. They returned for corresponding visit within the pre-specified visit window, e.g. 360 ± 30 days for the 12 Month Restenosis endpoint
2. They came back for an earlier or later scheduled or unscheduled visit that is after the corresponding visit window and the subject's vessel is patent and an earlier imaging visit shows the vessel is patent OR the subject's vessel is not patent and an earlier imaging visit shows the vessel is not patent

Events defined for the period of 12 months post-procedure follow up are reported for subjects with at least 390 days of follow-up or had 12-month visit within window (360±30 days) or with event to 390 days.

Subjects are included in the denominator for the image (restenosis) endpoint time frame if they returned for corresponding visit within the pre-specified visit window, e.g. 360 ± 30 days for the 12 Month Restenosis endpoint.

One (1) subject had a TVR, during which a balloon was inflated in the proximal segmental study stent. At that time the study stent was patent. Thus the TLR was non-clinically driven. This subject was censored from the primary patency analysis.
Lesion lengths greater than 140 mm were excluded from the trial and the longest available stent length was 150 mm.

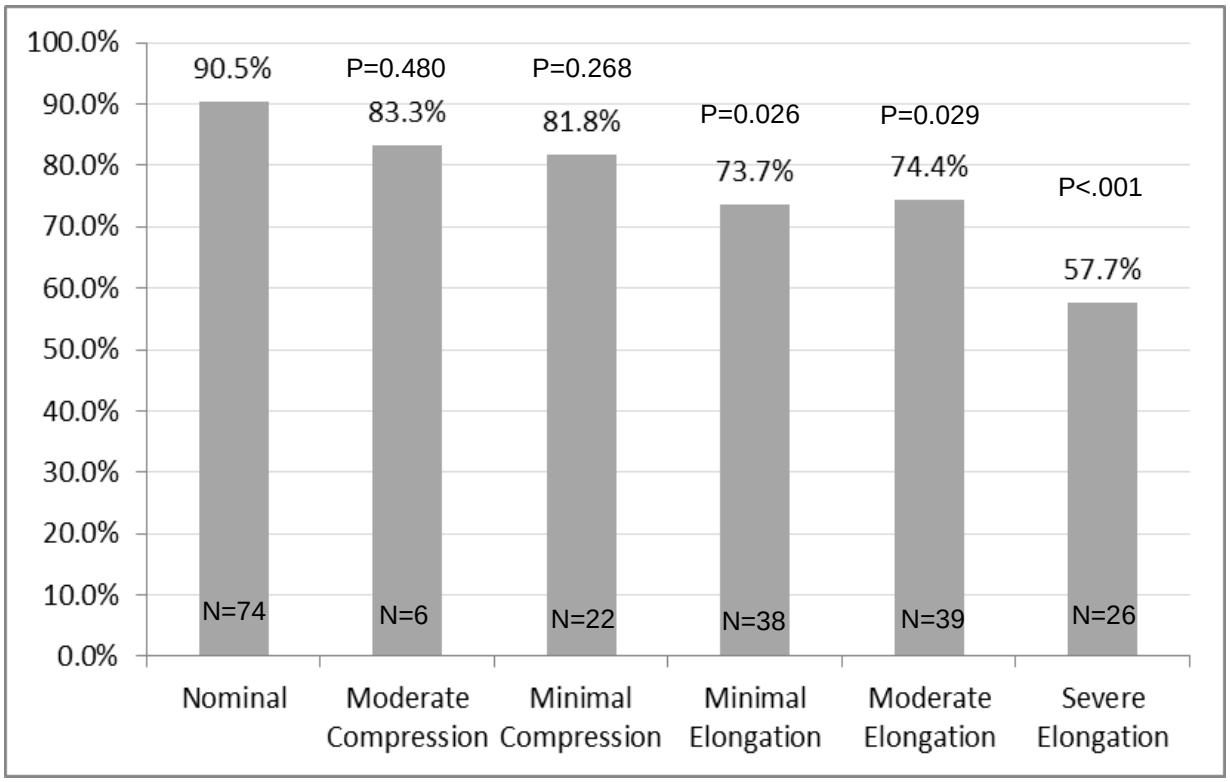
Post-Hoc Analysis of Deployed Stent Length

Compression (stacking) and elongation of the stent was detected in the SUPERB study. The impact of overall stent compression and elongation on the occurrence of primary patency in subjects undergoing SFA/PPA intervention with the Supera stent was evaluated by BIDMC Angiographic Core Laboratory. Procedural angiograms were analyzed at baseline after Supera stent implantation in 236 subjects who underwent single Supera stent implantation. There were 29/265 of ITT subjects' angiograms not included in the analysis due to a combination of multiple stent use, non-study stent use at the target lesion, or follow-up images that could not be assessed. Using an external calibration source, stent length was measured following implantation and compared to the labeled stent length.

- Nominal deployment is defined as the stent length upon deployment being within ±10% of labeled stent length
- Stent compression is defined as a percentage of measured deployed stent length shorter than labeled stent length

- Minimal stent compression is defined as deployed length shorter than labeled stent length by 11 to 20%
- Moderate stent compression is defined as deployed length shorter than labeled stent length by 21 to 40%
- Stent elongation is defined as a percentage of measured deployed stent length greater than labeled stent length
- Minimal stent elongation is defined as deployed length longer than labeled stent length by 11 to 20%
- Moderate stent elongation is defined as deployed length longer than labeled stent length by 21 to 40%
- Severe stent elongation is defined as deployed length longer than labeled stent length by greater than 41%

Figure 7: for Relationship of Stent Elongation to Primary Vessel Patency at 12 months – ITT, Single Stented Subjects



Note: N represents the number of subjects evaluable for the primary patency assessment. P-values indicate the statistical significance of the difference of the patency rates between each group and Nominal group.

As this figure demonstrates, a decrease in patency was observed when stents were deployed elongated. While this FDA-requested analysis was post-hoc and not powered to detect a difference, the greater amount of elongation

correlated to a significant reduction in patency at 12 months. In addition, the demographics and lesion characteristics were similar across all groups. Physicians should pay careful attention to deploy the stent to the appropriate dimensions to achieve the best possible clinical results.

Secondary Effectiveness Endpoint Analysis

The secondary effectiveness endpoints are summarized in **Tables 23** through **Table 25**, below,

Table 23: Acute Success

	N=264 subjects N= 265 segments
Device Success (Per Subject)	98.5% (257/261)
Technical Success (Per Segment)	100.0% (262/262)
Procedural Success (Per Subject)	100.0% (261/261)

Note:

Device success is the achievement of a final residual diameter stenosis of <50% (by QA), using the assigned treatment only.

Technical success is defined as <50% residual stenosis by Quantitative Angiography (QA) by any percutaneous method as determined by the Angiographic core laboratory.

Procedural success is defined as achievement of a final diameter stenosis of <50% (by QA) using any percutaneous method, without the occurrence of death, amputation or repeat revascularization of the target lesion during the hospital stay.

Table 24: Summary of Secondary Effectiveness Endpoints Secondary Effectiveness Endpoints	ITT Population (264 Subjects, 265 Segments)
Patency at 6 Months (PSVR < 2.0)	84.9% (191/225)
Patency at 6 Months (PSVR ≤2.4)	86.2% (194/225)
Patency at 12 Months (PSVR ≤2.4)	80.3% (183/228)
Target Lesion Revascularization - At 12 Months	11.1% (26/235)
Target Lesion Revascularization – At 24 Months	16.9% (36/213)
Target Vessel Revascularization - At 12 Months	13.2% (31/235)
Target Vessel Revascularization - At 24 Months	20.7% (44/213)
Improvement in the Rutherford-Becker Clinical Improvement Scale of ≥ one at 12 months	88.7% (204/230)
Improvement in the Rutherford-Becker Clinical Improvement Scale of ≥ one at 24 months	89.2% (181/203)

Note:
Subjects in the ITT Population are included in the clinical endpoint evaluation if:

1. They return for their corresponding visit within the window OR
2. They came back for a later scheduled or un-scheduled visit (i.e. a visit form is completed and the sponsor has documented information about their clinical status within the endpoint time frame) OR
3. The last contact date predated the endpoint time frame (they withdrew, were LTFU, died or exited the study for other reasons) BUT had an endpoint event within the endpoint time frame.

Events defined for the period of 12 months post-procedure follow up are reported for subjects with at least 390 days of follow-up or had 12-month visit within window (360 ± 30 days) or with event to 390 days.
Events defined for the period of 24 months post-procedure follow up are reported for subjects with at least 750 days of follow-up or had 24-month visit within window (720 ± 30 days) or with event to 750 days.
Subjects are included in the denominator for the image (restenosis) endpoint time frame if they returned for corresponding visit within the pre-specified visit window, e.g. 360 ± 30 days for the 12 Month Restenosis endpoint.
One (1) subject had a TVR, during which a balloon was inflated in the proximal segmental study stent. At that time the study stent was patent. Thus the TLR was non-clinically driven. This subject was censored from the primary patency analysis.
**Defined as: uninterrupted patency with no procedures performed on or at the margins of the treated segment, with no restenosis ≥ 50% as documented by DUS peak systolic velocity ratio ≥ 2.0 or > 2.4

Table 26 below provides a summary of the Rutherford/Becker Classification from pre-procedure through 24 months:

Table 26: Analysis of Rutherford Becker Scale at Baseline, 1 Month, 12 and 24 Months of Follow-Up – ITT Population

Rutherford Becker Clinical Category	Baseline	1 Month	12 Months	24 Months
(0) Asymptomatic – No Hemodynamically Significant Occlusive Disease	0.0% (0/264)	69.9% (181/259)	64.3% (148/230)	68.0% (138/203)

Rutherford Becker Clinical Category	Baseline	1 Month	12 Months	24 Months
(1) Mild Claudication	0.0% (0/264)	23.9% (62/259)	18.7% (43/230)	17.7% (36/203)
(2) Moderate Claudication	37.5% (99/264)	5.0% (13/259)	13.9% (32/230)	10.3% (21/203)
(3) Severe Claudication	57.2% (151/264)	1.2% (3/259)	2.2% (5/230)	2.0% (4/203)
(4) Ischemic Rest Pain	5.3% (14/264)	0.0% (0/259)	0.0% (0/230)	0.0% (0/203)
(5) Minor Tissue Loss, Focal Gangrene With Diffuse Pedal Ischemia	0.0% (0/264)	0.0% (0/259)	0.9% (2/230)	2.0% (4/203)
Limb Ischemia Improvement	NA	97.3% (252/259)	88.7% (204/230)	89.2% (181/203)

Note: Limb ischemia improvement is defined as an improvement in the Rutherford-Becker Clinical Improvement Scale of greater than or equal to one.

The majority of subjects had moderate-severe claudication (Rutherford Becker 2-3) at baseline. At 1, 12, and 24 months post procedure, a majority of subjects were asymptomatic (Table 24).

Table 27 below provides a summary of results of the ABI assessment from pre-procedure through 12 months.

Table 27: Ankle-Brachial Index

ABI on target limb	Baseline	1 month	6 months	12 months
Mean±SD (N)	0.7±0.2 (257)	1.0±0.2 (251)	0.9±0.2 (226)	0.92±0.22 (227)
Median	0.7	1.0	0.9	0.9
Min, Max	0.0,1.7	0.4,2.2	0.0,2.5	0.0,2.1

There was an overall improvement in ABI from a mean of 0.7 at baseline to 0.9 at 12 months. ABI data were not collected at 24 months.

3. Subgroup Analysis

a. Applicability to Pediatric Populations

The safety and effectiveness of the Supera® Peripheral Stent System was not studied in pediatric subjects in the SUPERB clinical study as peripheral artery disease is not typically found in the pediatric population.

b. Gender Sub-group Analysis

Primary endpoints through 12 months by gender are presented below in **Table 28**. The representation of females in the study (36.6%) is similar to

that of the general population with PAD and other interventional studies. The freedom from death, TLR or any amputation of the index limb to 30 (± 7) days post-procedure was 98.8% for males and 100% for females. The primary patency rate at 12 months was 82.6% for males and 72.6% for females. As shown in the tables below, relatively small differences in outcomes were observed for the primary safety and effectiveness endpoints between the sexes in this study and the results are considered comparable. Females did have lower freedom from TLR which may have been influenced by a smaller reference vessel diameter for females versus males, 4.54 ± 0.67 versus 5.21 ± 0.95, ($p<.001$) respectively.

Table 28. Primary Endpoints through 12 Months - By Gender

	Male (N=168 Subjects)	**Female (N=96 Subjects)**
Primary Safety Endpoint (30 ± 7 days)		
Freedom from Death, Target Lesion Revascularization (TLR) or any amputation of the index limb	98.8% (163/165)	100.0% (95/95)
Freedom from All Cause Death	99.4% (164/165)	100.0% (95/95)
Freedom from TLR*	99.4% (164/165)	100.0% (95/95)
Freedom from Amputation of the index	100.0% (165/165)	100.0% (95/95)
Effectiveness Endpoint 360 (± 30 days)		
Patency rate at 12 months (PSV Ratio < 2.0)	82.6% (119/144)	72.6% (61/84)
No Restenosis at 12 months**	86.8% (125/144)	86.6% (71/82)
Freedom from TLR to 12 months	92.5% (135/136)	83.1% (74/89)
Patency rate at 12 months (PSV Ratio ≤ 2.4)	83.3% (120/144)	75.0% (63/84)
No Restenosis at 12 months**	87.5% (126/144)	89.0% (73/82)
Freedom from TLR to 12 months	92.5% (135/146)	83.1% (74/89)

	Male (N=168 Subjects)	Female (N=96 Subjects)

Note:
Subjects are included in the clinical endpoint evaluation if:

1. They return for their corresponding visit within the window OR
2. They came back for a later scheduled or un-scheduled visit (i.e. a visit form is completed and the sponsor has documented information about their clinical status within the endpoint time frame) OR
3. The last contact date predated the endpoint time frame (they withdrew, were LTFU, died or exited the study for other reasons) BUT had an endpoint event within the endpoint time frame.

Specifically, events defined for the period of 30 days post-procedure follow up are reported for subjects with at least 37 days of follow-up or had 30-day visit within window (30±7 days) or with event to 37 days. Events defined for the period of 12 months post-procedure follow up are reported for subjects with at least 390 days of follow-up or had 12-month visit within window (360±30 days) or with event to 390 days.
Subjects are included in the denominator for the image (restenosis) endpoint time frame if:

1. They returned for corresponding visit within the pre-specified visit window, e.g. 360 ± 30 days for the 12 Month Restenosis endpoint
2. They came back for an earlier or later scheduled or unscheduled visit that is after the corresponding visit window and the subject's vessel is patent and an earlier imaging visit shows the vessel is patent OR the subject's vessel is not patent and an earlier imaging visit shows the vessel is not patent

*One (1) subject had a TVR, during which a balloon was inflated in the proximal segmental study stent. At that time the study stent was patent. Thus the TLR was non-clinically driven. This subject was censored from the primary patency analysis.
**No stenosis ≥ 50% diameter stenosis.

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 145 investigators of which none were full-time or part-time employees of the sponsor and 7 investigators (at 6 sites) had disclosable financial interests/arrangements as defined in 21 CFR 54.2(a), (b), (c) and (f) and described below:

- Compensation to the investigator for conducting the study where the value could be influenced by the outcome of the study: none
- Significant payment of other sorts: 3
- Proprietary interest in the product tested held by the investigator: none
- Significant equity interest held by investigator in sponsor of covered study: 5

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

XI. PANEL MEETING RECOMMENDATION

In accordance with the provisions of Section 515(c) (2) of the act as amended by the Safe Medical Devices Act of 1990, this PMA was not referred to the Circulatory Systems Devices Panel, an FDA advisory committee, for review and recommendation because the information in the PMA substantially duplicates information previously reviewed by this panel.

XII. CONCLUSIONS DRAWN FROM CLINICAL STUDIES

A. Safety Conclusions

Among the 264 ITT subjects, 99.2% (258/260, 95% lower CL 97.7%) met the primary safety endpoint (i.e., freedom from a composite of all death, TLR, or any amputation of the index limb to 30 days). This rate was higher than the pre-specified performance goal of 88% with statistical significance ($p<0.001$). Therefore, the primary safety endpoint was met.

B. Effectiveness Conclusions

The primary effectiveness endpoint, primary stent patency, was evaluated in all enrolled subjects with evaluable 1-year data, and was achieved in 78.9% (180/228) of the subjects (95% lower CL 74.2%). This rate is greater than the pre-specified performance goal of 66%, with statistical significance ($p<0.001$). Therefore, the primary effectiveness endpoint was met.

C. Benefit-Risk Conclusions

The probable benefits of the device are also based on data collected in a clinical study conducted to support PMA approval as described above. The probable benefit of the Supera® Peripheral Stent System of improving the patient symptoms and quality of life outweigh the probable risks associated with use of the device.

Additional factors to be considered in determining probable risks and benefits for Supera® stent system included:

- Patient follow-up was satisfactory and with limited missing data. Follow-up for the PMA was 24 months, with some patients out to 36 months. Follow-up will continue to 36 months for all patients, to evaluate the longer term device performance, such as the duration of the benefit and long term adverse event rates.

- The pivotal study was a multi-center study conducted in the United States. The results obtained should not differ from the post-market performance. Additional long-term data will be obtained.

- Most patients with the disease have symptoms only, but some patients may have more extensive disease involvement. The device treats the hemodynamic consequences of the disease to improve perfusion and function. The disease is chronic and affects the mobility of the patient and the quality of life. It is treatable but not curable.

- There are alternative treatments available, but this treatment is highly valued by patients and preferred to the alternatives because it improves their quality of life with lesser need for repeat procedures compared to a performance goal based upon angioplasty results without stenting.

- Patient risk is minimized by limiting use to operators who have the necessary training to use the device safely and effectively and by adherence to recommended periprocedural medication regimens.

In conclusion, given the available information above, the data support that the probable benefits outweigh the probable risks for using the device for improving luminal diameter in the treatment of patients with symptomatic de novo or restenotic lesions or occlusions in native vascular disease of the above-the-knee femoropopliteal arteries with reference vessel diameters of 4.0 mm to 6.5 mm and total lesion lengths up to 140 mm.

D. Overall Conclusions

The clinical and non-clinical data in this application provide a reasonable assurance that the device is safe and effective. The pre-specified safety and effectiveness endpoints of the SUPERB clinical trial were met, and the study results are similar to the results for other US marketed stents intended for use in patients with SFA and proximal popliteal lesions. Although 20 and 30 mm long stents were not included in the SUPERB trial, sufficiently robust pre-clinical data, complaint analyses and the specific design characteristics of the delivery system with respect to the delivery and locking mechanism were used to support approval of these stent lengths. Therefore, it is reasonable to conclude that the benefits of use of the device for the target population outweigh the risk of illness or injury when used as indicated in accordance with the labeling and Instructions for Use (IFU).

XIII. CDRH DECISION

CDRH issued an approval order on March 28, 2014. The final conditions of approval cited in the approval order are described below.

In addition to the general conditions outlined, the sponsor must conduct a post-approval study to evaluate the long-term safety and effectiveness of the Supera Peripheral System in the pivotal study cohort through 3 years post implantation as outlined below.

1. *SUPERB Extended Follow-Up Study*: The study will be a continued follow-up of patients treated with the Supera peripheral stent system in the prospective, multicenter, non-randomized SUPERB clinical study.

   The primary safety and effectiveness objective is to assess the composite event of amputation and clinically-driven target lesion revascularization (TLR) at 2 and 3 years post implant as assessed at clinical visits.

   The secondary safety objective is to assess stent fracture rate by X-ray (defined as type I, II, III, IV or V), the composite endpoint of death, amputation and TLR, adverse and serious adverse events, and unanticipated adverse events through 2 and 3 years. The secondary effectiveness objective is to evaluate the improvement in limb ischemia as assessed by the Rutherford Becker Scale at 2 and 3 years.

   The study population will be comprised of the 256 subjects (212 ITT and 44 roll-in) remaining in the premarket cohort who will be followed out to 2 and 3 years post implant. Assuming a lost to follow-up rate of 15% per year, and a safety event rate of 25-30% at 3 years, an evaluable sample size of 175 subjects will assure that the point estimates for the safety endpoint at 3 years post procedure is estimated with reasonable precision, i.e. the ratio of the upper one-sided 95% confidence limit and the point estimate is ≤ 1.25.

   The study outcomes will be summarized and reported separately for the intent-to-treat (ITT) and roll-in populations. The safety and effectiveness endpoints will be evaluated using Kaplan-Meier analysis, counts, percentages and 95% CI. Stent fracture, adverse events, serious adverse events, and unanticipated adverse events will be reported descriptively.

The applicants manufacturing facility was inspected and found to be in compliance with the device Quality System (QS) regulation (21 CFR 820).

XIV. APPROVAL SPECIFICATION

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.